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“I don’t want to manage it, I want to get rid of it”:

**A narrative analysis of living with chronic plaque psoriasis,
and an investigation into vitamin D as a treatment**

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Abstract

As a chronic skin disease, plaque psoriasis can cause significant psychosocial, emotional and physical burden. Psoriasis sufferers perceive others as lacking understanding around what it is like to live with this condition, and there has been little research exploring the experience of psoriasis in depth. The burden of psoriasis can be compounded by the difficulty of treating it, and the inconveniences, side effects and risks of available treatments, suggesting the importance of finding a safe, effective and convenient treatment for psoriasis. Vitamin D and psoriasis have a long-standing relationship, with topical vitamin D analogues used to treat mild-to-moderate disease, and observational studies suggesting an association between higher systemic vitamin D (serum calcidiol) concentrations and less severe psoriasis. These findings suggest vitamin D₃ supplements, which raise serum calcidiol concentrations, might improve psoriasis. In this thesis, two studies were conducted to address the limited in-depth understanding of the experience of psoriasis, and the need for a safe, effective treatment, respectively. The aims were 1) to gain a deeper understanding of the experience of living with psoriasis; and 2) to investigate whether oral vitamin D₃ supplements can effectively treat psoriasis.

For 1), data from semi-structured interviews with 10 men and women with psoriasis was analysed using narrative analysis. Narrative trajectories involving three predominant narrative forms shaped participants' stories: *restitution*, where the focus was on overcoming psoriasis through trying to find an effective treatment or cure; *chaos*, where psoriasis was experienced as overwhelming and brought about a sense of hopelessness, and *resignation*, which was centred on begrudgingly accepting psoriasis in order to be able to get on with life. Participants had different narrative trajectories and shifted between forms over time, with the nature of experience linked with the relative stability and severity of a person's psoriasis and their beliefs about their ability to manage it.

For 2), a randomised, double-blinded, placebo-controlled trial was conducted with 101 participants ≥ 18 years allocated to 100,000 International Units (IU) vitamin D₃/month ($n = 67$)

for 12 months (200,000 IU at baseline), or an identical placebo ($n = 34$). Psoriasis severity (Psoriasis Area and Severity Index [PASI]) and serum calcidiol concentrations were assessed at 3-monthly intervals. The primary outcome was the difference in PASI between treatment and placebo over time, assessed using a linear mixed model. Psoriasis severity did not differ between groups at any time (group $F(1, 106) = 0.59, p = 0.44$, group*time $F(4, 370) = 0.52, p = 0.72$). Yet these findings are inconclusive, as serum calcidiol significantly increased from baseline in both the treatment and the placebo group, and a mild improvement in PASI score from baseline also occurred in each group. A non-predetermined secondary analysis was performed by assessing the strength of the relationship between serum calcidiol concentration and PASI score across the whole sample, and this showed a significant inverse relationship between the two variables, in that elevation of serum calcidiol concentration by increments from 25 nmol/L to 125 nmol/L was associated with very mild decreases in PASI (estimated range of decrease 0 – 2.6; $p = 0.002$). Therefore, despite being unable to determine a benefit of vitamin D₃ supplements for psoriasis, these findings support the notion of a potential benefit of increasing serum calcidiol concentrations across the psoriatic population.

In conclusion, this thesis offers insight into ways in which people can experience psoriasis over time: as a temporary and fixable condition that must be overcome, as an overpowering force and source of significant suffering, and as a permanent condition that is reluctantly accepted. As the findings emphasise the negative influence of the difficulties around managing and treating psoriasis on the experience of psoriasis, they provide further support for the need for an effective, safe and convenient treatment. While the findings were inconclusive in regards to whether oral vitamin D₃ can help people to manage their psoriasis, the significant association between psoriasis severity and systemic vitamin D concentration supports continued research into this potential.

I was engaged in a relentless physical assault on my symptoms, at war with my skin . . . and inevitably losing. The disease and its treatment merged, combining inextricably to impact upon my personal experience and social identity; a sad fact that both were in effect demeaning.... If my self-esteem was affected by the disease, the treatment made the damage worse (Jobling, 2007, pp. 953-4).

Preface

The origins of this thesis began in an interest in vitamin D, and the subsequent decision to conduct a randomised controlled trial investigating whether vitamin D could effectively treat psoriasis. I had also intended to assess participants' quality of life and the extent they suffered from physical disability because of their psoriasis, and I was going to do so by using quantitative questionnaires over the five times I met with each participant over their year of enrolment in the trial. Yet, once I began to meet with participants, out came telling anecdotes, outlooks on life, conversational snippets that alluded to formative experiences but never quite explained them. I sensed that some participants lived in the throes of the burden of psoriasis, while those who did not had left the weight of their concerns somewhere in the past. Psoriasis seemed much more than a disease of the skin, of the body; it appeared to have shaped the lives of many of my participants through impacting their self-perception and experiences. I also suspected that the comments that were shared did not usually reach the open, yet here, in the privacy of the researcher/participant relationship, they were inching their way to the surface. I reflected on my research project: in the hands of Likert-scaled questionnaires, these stories would disappear amongst the coding. I wanted to hear more, to look deeper, and in some sense, to provide an anonymous voice for these experiences. I wanted to know how having psoriasis affects a person's life through impacting the experiences that they navigate over time, each inevitably leaving its mark somehow etched in the present day. I was also aware that available psoriasis treatments are not always effective, can be inconvenient, and have risks and side effects, and therefore can compound the reduced quality of life that is frequently seen in people with psoriasis. I wondered, what are the implications of the drawbacks of treatments on a personal level? Why is it so important that I investigate the potential of vitamin D (which is safe, easily administered and has no side effects) as a treatment for psoriasis? And thus, my thesis metamorphosed, from a story based around serum vitamin D concentrations and somewhat objective skin assessments, to include a story about people, their experiences of living with psoriasis and their search for effective treatments, all of this adding meaning to my

investigation into the treatment potential of vitamin D. This thesis is therefore comprised of two complementary parts, each aligning with one of the overall aims as set out below. In order to conduct both parts of this research it has been necessary to take an inter-disciplinary approach to this thesis, using narrative theory and analysis based on qualitative research traditions alongside quantitative methods. My hope is that this approach provides a deeper, richer understanding of the impact of psoriasis on people's lives, and illustrates why it is so important to find a treatment for psoriasis that is free of risks and side effects.

Aims of Thesis

This thesis has two distinct aims, which are approached as two separate research studies. The specific aims of each study are as follows:

Study One: To gain a deeper understanding of how people experience living with psoriasis through identifying and analysing the narratives they use to describe their experiences.

Study Two: To determine whether oral vitamin D₃ supplementation is an effective treatment for psoriasis.

This thesis is presented over seven chapters. Chapter 1 introduces the thesis as a whole, presents a rationale for each study and demonstrates how these studies have complementary aims that fit together as part of one thesis. Chapter 2 provides an overview of psoriasis in order to provide context for the aims of this thesis. This overview discusses the characteristics of psoriasis (both clinical and at a cellular level), the numerous co-morbidities it has been associated with, and the limited body of knowledge relating to the causes and triggers of psoriasis. It also includes a discussion of the treatments that are currently available for psoriasis and their advantages and disadvantages.

Chapter 3 presents the background, theoretical and methodological approaches, and the methods of Study One: A narrative analysis of living with psoriasis. It opens with a critical discussion of the literature as it pertains to the experience of living with psoriasis, to provide an understanding of the broad range of issues that relate to living with psoriasis and thereby providing the background for the present study. This is followed by a presentation of the epistemological and methodological approaches for this research, including a critical discussion of the approaches taken in previous studies about the experience of psoriasis in order to justify the need for a narrative approach. This chapter concludes with a description of the methods used in the present study, including the process that was followed to conduct the narrative analysis.

Chapter 4 presents the findings of Study One, followed by a discussion of these findings in the context of the wider literature.

Chapter 5 presents the background, methodological approach and methods used in Study Two: An investigation into the potential of oral vitamin D₃ supplementation as a treatment for psoriasis. It begins with an overview of vitamin D, including its various functions, sources and an in-depth discussion of required levels and intakes. This is followed by a critical discussion of the literature regarding the relationship between psoriasis and vitamin D, arguing for the need to investigate the potential for vitamin D₃ supplements for the treatment of psoriasis. This is followed by a description of the methods and procedures used in the trial.

Chapter 6 presents the findings of Study Two, and a discussion of these findings in relation to the wider literature.

Finally, an overview of the findings of this thesis, a discussion of their implications and the original contributions that this thesis offers are presented in Chapter 7.

Acknowledgements

As I reach the point of culmination of work on this thesis, and conduct the necessary revisions of a research story I have lived and grappled with for many years, I have had the chance to reflect on, and sometimes, it feels, to even re-live all the rather amazing experiences that have formed part of the PhD experience for me. Most of all, however, it has been the people who have stayed with me; first of all, the many, many wonderful participants who gave up their precious time to come and help me find out whether there might be hope for psoriasis in vitamin D. You showed me why this research was important and why I had to keep going, and inspired me to look deeper into the experience of psoriasis. Equally, to the wonderful people who so openly and generously shared their stories and experiences about living with psoriasis, my deepest thanks; you taught me so much through your stories, and I hope I have been able to do you justice in my analysis. Thank you all so much for taking part; without you, this thesis would not be.

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Table of Contents

Abstract	i
Preface	v
Aims of thesis	vi
Acknowledgements	viii
List of tables	xvi
List of figures	xvii
List of abbreviations	xviii
1. Introduction.....	1
2. An Overview of Psoriasis	12
2.1. Background and definition.....	12
2.2. Clinical features and sub-classifications	14
2.3. Co-morbidities	17
2.4. Epidemiology	22
2.5. Aetiology	23
2.5.1. Genetic factors	23
2.5.2. Environmental triggers	24
2.6. Processes involved in plaque formation	24
2.7. Role of the immune system	27
2.8. Treatments	29
2.8.1. Topical treatments.....	33
2.8.2. Phototherapy	35
2.8.3. Conventional systemic treatments	36
2.8.4. Biological therapies	37
2.9. Summary and conclusions	38
3. Study One: The Experience of Living with Psoriasis	40
3.1. Living with psoriasis	40
3.1.1. The impact of psoriasis on quality of life	41
3.1.2. The physical burden of psoriasis	44
3.1.3. The psychosocial burden of psoriasis	46
3.1.4. The impact of psoriasis on work, career and education.....	52
3.1.5. The burden of psoriasis treatment and the struggle for control	53
3.1.6. Experiences with healthcare providers	55

3.1.7.	Adjustment to psoriasis.....	56
3.1.8.	Conclusion	59
3.2.	Methodology	60
3.2.1.	Epistemological perspective	61
3.2.2.	Methodological approaches of past research into the experience of psoriasis	62
3.2.3.	Definition of social constructionism.....	74
3.2.4.	Narrative	76
3.2.5.	Narrative and social constructionism.....	79
3.2.6.	Narrative and illness	81
3.2.7.	Understanding narratives about living with psoriasis from a social constructionist perspective in this research	83
3.3.	Methods.....	86
3.3.1.	Recruitment.....	86
3.3.2.	Participants.....	88
3.3.3.	Ethics	88
3.3.4.	The interview process	89
3.3.5.	Transcription.....	93
3.3.6.	Narrative analysis.....	93
3.3.7.	Reflexivity	97
4.	Study One: Findings and Discussion.....	105
4.1.	Findings.....	105
4.1.1.	The restitution narrative.....	105
4.1.2.	The resignation narrative	110
4.1.3.	The chaos narrative.....	117
4.1.4.	The quest narrative.....	123
4.2.	Discussion	129
4.2.1.	The persistence of the restitution narrative in the face of no cure	129
4.2.2.	Loss of control, identity and the chaos narrative	133
4.2.3.	The resignation narrative: Acceptance that is at most, begrudging	135
4.2.4.	Narrative trajectories and the role of perceived stability and severity of psoriasis.....	139
4.2.5.	Consequences of the incongruence between psoriasis and societal ideals around appearance.....	141
4.2.6.	The challenge of creating value from psoriasis: The lack of quest narratives.....	142
4.3.	Conclusion	145

5. Study Two: Assessing the Efficacy of Vitamin D₃ Supplements for Treating	
Psoriasis	147
5.1. Vitamin D	147
5.1.1. Background.....	147
5.1.2. Definition of vitamin D.....	148
5.1.3. Physiological functions of vitamin D	149
5.1.4. Forms of vitamin D.....	149
5.1.5. Endogenous synthesis of vitamin D ₃	149
5.1.6. Vitamin D levels in New Zealand.....	151
5.1.7. Factors affecting endogenous synthesis of vitamin D	152
5.1.8. Dietary sources of vitamin D	153
5.1.9. Physiological factors affecting response to supplementation and vitamin D status.....	155
5.1.10. Definitions of vitamin D status and recommended intakes	156
5.2. Vitamin D and psoriasis	161
5.2.1. Vitamin D and keratinocytes	162
5.2.2. Vitamin D and the immune response.....	163
5.2.3. Psoriasis and vitamin D receptor polymorphisms	164
5.2.4. Psoriasis and topical vitamin D and its analogues	164
5.2.5. Psoriasis and oral calcitriol	165
5.2.6. Serum calcidiol concentrations in the psoriatic population	167
5.2.7. Associations between serum calcidiol concentrations and psoriasis severity	170
5.2.8. Psoriasis and oral vitamin D	172
5.2.9. Summary and conclusion.....	173
5.3. Methods	174
5.3.1. Recruitment and screening.....	174
5.3.2. Study design.....	175
5.3.3. Ethics and trial registration	177
5.3.4. Study procedures.....	177
5.3.5. Vitamin D ₃ and placebo capsules	183
5.3.6. Analysis of blood samples	184
5.3.7. Data handling and statistical analysis	185
5.3.8. Communication of results to participants	190
5.3.9. Funding	190
6. Study Two: Findings and Discussion	191
6.1. Findings	191

6.1.1.	Participant characteristics	191
6.1.2.	Psoriasis severity (PASI scores)	191
6.1.3.	Systemic vitamin D (serum calcidiol) concentrations	193
6.1.4.	Relationship between psoriasis severity and systemic vitamin D	198
6.1.5.	Compliance	200
6.1.1.	Safety	202
6.2.	Discussion	203
6.2.1.	Increased serum calcidiol and a reduction in PASI in both groups	203
6.2.2.	The significant inverse relationship between serum calcidiol and PASI.....	204
6.2.3.	The magnitude of estimated average improvement, and heterogeneity in the relationship between serum calcidiol and PASI	205
6.2.4.	Consideration of the serum calcidiol concentrations achieved by participants ...	207
6.2.5.	The presence of a relationship between serum calcidiol and PASI across the range of serum calcidiol concentrations.....	207
6.2.6.	The question of how calcidiol in serum might benefit psoriasis	208
6.2.7.	Serum calcidiol concentrations in people with psoriasis compared to the wider population.....	208
6.2.8.	Strengths and limitations of this research	209
6.3.	Conclusion	212
7.	Conclusion	214
8.	References.....	226
9.	Appendices	
	Study One	253
	Appendix 1. Email advertisement.....	254
	Appendix 2. Information sheet	255
	Appendix 3. Ethics approval.....	257
	Appendix 4. Consent form.....	258
	Appendix 5. Semi-structured interview guide	259
	Appendix 6. Participants' backgrounds, psoriasis histories and abridged storylines	261
	Study Two.....	273
	Appendix 7. Recruitment material provided to medical centres and dermatology clinics	274
	Appendix 8. Media releases for study	278
	Appendix 9. Recruitment email to Massey University Nutrition Dept database.....	282
	Appendix 10. Information sheet	283
	Appendix 11. Screening questionnaire	288

Appendix 12. Email communication with participants with regards to recruitment and enrolment.....	294
Appendix 13. Ethics approval.....	296
Appendix 14. SCOTT approval.....	299
Appendix 15. Consent form.....	301
Appendix 16. Personal details form.....	303
Appendix 17. Demographics form.....	304
Appendix 18. Psoriasis and medical history form (visit 1).....	306
Appendix 19. PASI scoring sheet.....	311
Appendix 20. PASI scoring visual reference guide.....	312
Appendix 21. Post-Visit 1 letter for participants	313
Appendix 22. Welcome letter for participants explaining capsule protocol.....	314
Appendix 23. Capsule labels	315
Appendix 24. Psoriasis and medical history form (visit 2).....	316
Appendix 25. Exit questionnaire for final study visit.....	320
Appendix 26. Letter for participants explaining what happens after their final visit.....	324
Appendix 27. Vitamin D and placebo capsule certificates of analysis.....	325
Appendix 28. Letter for participants advising individual and study results	327
Appendix 29. Unpublished journal article: Response to vitamin D ₃ supplementation and predictors of change.....	333

List of Tables

Table 1	Sub-classifications of plaque psoriasis.....	18
Table 2	Treatments available for chronic plaque psoriasis in New Zealand.....	30
Table 3	Previous research using a qualitative approach to understand the experience of psoriasis.....	65
Table 4	Participant characteristics and treatment history	90
Table 5	Characteristics of narrative forms identified in experiences of psoriasis.....	104
Table 6	Vitamin D content of selected foods in New Zealand.....	154
Table 7	Examples of vitamin D ₃ supplements available in New Zealand.....	155
Table 8	Comparison between the Institute of Medicine and the Endocrine Society definitions of vitamin D status and recommended intakes	161
Table 9	Participant characteristics at baseline by group.....	192
Table 10	PASI scores over 12 months by group	195
Table 11	Percentage of participants achieving $\geq 50\%$ improvement in PASI from baseline.....	196
Table 12	Serum calcidiol concentrations over 12 months by group	196
Table 13	Percentage of participants in each group according to vitamin D status.....	197
Table 14	Linear mixed model beta-coefficients and 95% confidence intervals for variables associated with log-transformed PASI score	199
Table 15	Estimated decreases in PASI scores at increments of change in serum calcidiol concentration	201

List of Figures

Figure 1	The clinical appearance of psoriasis	15
Figure 2	Histopathological features of psoriasis.....	26
Figure 3	Different narrative trajectories in participants' experience of living with psoriasis.....	106
Figure 4	Pathway of vitamin D metabolism	150
Figure 5	Flow diagram of participant numbers through different phases of the study	176
Figure 6	Predicted vs. residual plots for the primary outcome model	187
Figure 7	Predicted vs. residual plots for the model assessing the relationship between PASI and serum calcidiol concentration	189
Figure 8	Mean serum calcidiol concentrations over 12 months in each group.....	197
Figure 9	Partial residual plot showing the association of serum calcidiol concentration with PASI score	198
Figure 10	Frequency of correlations between log-transformed PASI and serum calcidiol concentration across all participants	202

List of Abbreviations

1 α -OHase	1-alpha-hydroxylase
25-OHase	25-hydroxylase
7-DHC	7-dehydrocholesterol
BIA	Bioelectrical impedance analysis
BMI	Body mass index
BSA	Body surface area
BUVB	Broadband ultraviolet-B
CI	Confidence interval
CRP	C-reactive protein
CV	Coefficient of variation
DBP	Vitamin D binding protein
ES	Endocrine Society
hsCRP	High-sensitivity C-reactive protein
IFN	Interferon
IL	Interleukin
IOM	Institute of Medicine
IU	International units
MED	Minimum erythema dosage
mRNA	Messenger ribonucleic acid
NSAIDs	Non-steroidal anti-inflammatory drugs
NUVB	Narrowband ultraviolet-B
OR	Odds ratio
OV/BV	Osteoid volume per bone volume
PASI	Psoriasis Area and Severity Index
PSORS1	Psoriasis susceptibility locus 1
PUVA	Psoralen and ultraviolet-A
RXR	Retinoid X receptor
SD	Standard deviation
Th	T-helper
TNF	Tumour necrosis factor
Treg	Regulatory T-cells
UK	United Kingdom
US	United States
UVA	Ultraviolet-A
UVB	Ultraviolet-B
VDR	Vitamin D receptor

1. Introduction

Psoriasis is a skin condition that has significant implications for sufferers in terms of general wellbeing and enjoyment of life. Known more specifically as chronic plaque psoriasis, it is a non-contagious inflammatory disease that results in distinctive lesions ('plaques') on the skin. It is one of the most common dermatological conditions, affecting between 2% and 5% of the Western world (Parisi, Symmons, Griffiths, Ashcroft, & IMPACT project team, 2013), which translates to an estimated 95,000 to 236,000 people in New Zealand in 2016 (Statistics New Zealand, 2016). The characteristic plaques of psoriasis are reddened, raised and well-demarcated patches of skin covered in silvery-white flaky scales (Griffiths & Barker, 2007). They can appear on any part of the body, but are most commonly found in areas that are often publicly exposed such as the elbows and knees (Griffiths & Barker, 2007; Luba & Stulberg, 2006). The majority of people also develop psoriasis on the scalp (Boehncke & Schön, 2015), which usually involves the prolific flaking of skin throughout hair, and onto clothing and elsewhere (Renton, 2014). The severity of psoriasis varies considerably amongst people, and within the same person over time, ranging from one or two plaques in very mild psoriasis, to a high percentage of skin coverage in severe cases (Griffiths & Barker, 2007). Its recalcitrant nature also makes it one of the most difficult skin conditions to manage, and affected individuals often swing in and out of remission in an unpredictable fashion (van de Kerkhof & Vissers, 2004).

Plaques are formed *via* a process involving the hyperproliferation and abnormal differentiation of keratinocytes (the predominant type of skin cell in the epidermis), the formation of new blood vessels (angiogenesis) in the dermal layer of skin, and an infiltration of inflammatory cells into the epidermis and dermis (Schön & Boehncke, 2005). As plaques are the most distinctive sign of psoriasis, it was once thought to be a benign condition limited to the skin (Baker et al., 2016). However, the definition of psoriasis has since evolved so that it is now considered a systemic disease that carries an increased risk of serious co-morbidities such as cardiovascular disease, metabolic syndrome and some cancers (Baker et al., 2016). Some

people with psoriasis also develop psoriatic arthritis, a unique, painful and debilitating arthritis, with the estimated prevalence among those with psoriasis varying from 6% to 42% (Gladman, Antoni, Mease, Clegg, & Nash, 2005). Despite recent advances in understanding of the pathophysiology of psoriasis, much about psoriasis remains unknown, most notably a complete understanding of its aetiology and natural history; that is, it cannot yet be said exactly why those with psoriasis have developed the disease, nor can the course of psoriasis be determined (Ryan et al., 2014). As psoriasis can develop at any time of life (Griffiths & Barker, 2007), and as no cure has been identified (Korman, Zhao, Pike, Roberts, & Sullivan, 2016) and treatments are not often able to provide full clearance (Strober et al., 2016), people must live with the condition over the long-term, and often over a lifetime (Vaidya, Anderson, & Feldman, 2015).

While psoriasis can be physically challenging, its impact on psychological and social wellbeing is often considered to be the most detrimental aspect of the disease, even in those with clinically mild disease (Stern, Nijsten, Feldman, Margolis, & Rolstad, 2004). On average, quality of life in people with psoriasis is significantly reduced compared to the wider population, to a degree that is comparable to those with major chronic diseases such as cancer, arthritis and depression (Rapp, Feldman, Exum, Fleischer, & Reboussin, 1999). This impact on quality of life can be partially understood in relation to feelings or overt experiences of stigmatisation due to the appearance of psoriasis, which are experienced by the majority of people with psoriasis at some point in their lives (Baker, Foley, & Braue, 2013; Hrehorow, Salomon, Matusiak, Reich, & Szepietowski, 2012). Skin diseases such as psoriasis have historically been associated with danger and even disgrace, bringing connotations of ill hygiene and impurity and fears of contagion (Jobling & Naldi, 2006). While such assumptions around psoriasis are false, stigma has nonetheless persisted, and people with psoriasis even feel shame and guilt at the thought of having offended others with their appearance (Jobling & Naldi, 2006). Stigmatisation in relation to psoriasis includes instances of feeling stared at, receiving unequal treatment or even being excluded from public facilities due to others' fears that they are contagious (Hrehorow et al., 2012; Krueger et al., 2001; Nash, McAteer, Schofield, Penzer, & Gilbert, 2015), and the

relationship between psoriasis severity and quality of life has been shown to be almost completely mediated by feelings and experiences of stigmatisation (Vardy et al., 2002). Similarly, psychological morbidity in psoriasis, such as embarrassment, shame, self-consciousness, low self-esteem, depression and anxiety has been related to feelings of being scrutinised and judged by others on the basis of appearance (Magin, Adams, Heading, Pond, & Smith, 2009a). To try and minimise such consequences, people with psoriasis commonly avoid participating in normal, everyday activities in which others might see their skin, such as sports and social activities, and visiting public swimming pools and gyms (Anstey, McAteer, Kamath, & Percival, 2012; Gupta & Gupta, 1995; Nash et al., 2015), limiting their ability to enjoy a normal, active life. Furthermore, a considerable majority of those with psoriasis choose to keep their condition hidden from the general public, and some even hide it from their family or partner (Baker et al., 2013). The perceived lack of understanding that surrounds psoriasis is illustrated by survey results from the United Kingdom (UK) in which nearly half of 1760 respondents felt that people were not understanding towards their psoriasis, and 84% felt that there was a general lack of understanding about psoriasis amongst the wider public (Anstey et al., 2012). A recent study in the United States (US) has also emphasised public misconceptions surrounding psoriasis, with nearly 61% of participants ($n = 56$) shown unidentified pictures of psoriasis believing that it had an infectious cause (Donigan, Pascoe, & Kimball, 2015). Additionally, misunderstanding around psoriasis may also arise from the perception that psoriasis is 'merely' a skin issue, and there may therefore be some corresponding insensitivity around the consequences it has for the sufferer. Because people with psoriasis are not 'sick', they may not necessarily be privy to the same degree of empathy as those who face more serious illnesses (Jobling & Naldi, 2006). Regardless of its origins, those who feel a lack of understanding from others in relation to their experience of living with psoriasis have a greater tendency to feel that their lives are negatively dictated by psoriasis (Bewley, Burrage, Ersser, Hansen, & Ward, 2014). The consequences of this can be profound, including such difficulties as forming and sustaining friendships and relationships, and limiting people from fulfilling their potential in their work lives, in the pursuit of education, and in their lives in general (Anstey et

al., 2012; Kimball et al., 2010; Warren, Kleyn, & Gulliver, 2011).

Some psoriasis patients also perceive a lack of empathy from healthcare professionals involved in the treatment of their psoriasis, feeling that doctors and other healthcare professionals do not appreciate the impact that psoriasis can have on their lives (Bewley et al., 2014; Ersser, Cowdell, Latter, & Healy, 2010; Nelson, Barker, Griffiths, Cordingley, & Chew-Graham, 2013a; Nelson, Chew-Graham, Griffiths, & Cordingley, 2013b). In another recent UK survey, 30% agreed with the statement “I don’t think my doctor takes my psoriasis very seriously”, and in a qualitative component, participants shared that they did not feel their doctors understood the seriousness of psoriasis, particularly the non-physical aspects (Bewley et al., 2014). Specifically, people with psoriasis have described a lack of acknowledgment from their healthcare practitioners of the stress, distress, social stigma and feelings of lack of control that they struggle with as a result of their psoriasis, and how some doctors even block opportunities for emotional disclosure, causing the patient to feel reluctant to raise such issues (Nelson et al., 2013b). This lack of acknowledgement might be due to a misalignment between how healthcare practitioners perceive the lived experience of psoriasis and how it is actually experienced by the patient (Nelson et al., 2013a); regardless, it can compound the already significant strain of living with psoriasis (Nelson et al., 2013b). Although the less-visible impact of psoriasis has become better appreciated in recent years, and it is now recommended that assessments of psoriasis severity take into account patients’ perceived burden of psoriasis on daily life (Baker et al., 2016), it is clear that there is still room for greater gains to be made in understanding what it is like to live with psoriasis, and that there is the potential for great benefit if such an increase in understanding occurs.

Because there is no cure for psoriasis, the aim of treatment is to try and minimise the extent of psoriasis and to keep it under control, to the extent that any impact on quality of life is also at an acceptably low level (Baker et al., 2016; de Korte, Sprangers, Mommers, & Bos, 2004). It is therefore usually a lifelong condition that must be managed, often on a daily basis (Vaidya et al., 2015). Several treatment options for psoriasis are currently available, with mild psoriasis

treated with various topical therapies, and moderate-to-severe psoriasis treated with phototherapy and/or conventional systemic or injectable biologic treatments (Van Cranenburgh, De Korte, Sprangers, De Rie, & Smets, 2013). However, although there is a range of different treatment options, psoriasis can be difficult to manage, with treatment efficacy varying widely between people and even within the same person over time (Bewley & Page, 2011). Furthermore, each of the treatment types available for psoriasis is also associated with inconvenience and/or side effects, some of which pose a serious risk to health (Boehncke & Schön, 2015; Cohen, Baron, & Archer, 2012; Menter et al., 2009). Thus, for some people, treatments designed to improve psoriasis can actually further contribute to the burden of living with the condition (Pariser et al., 2016). Topical corticosteroids are the most commonly prescribed topical treatment for psoriasis, yet can be inconvenient to use and can cause thinning of the skin, stretch marks and a risk of rebound upon discontinuation, and often become ineffective with continual use (Mason, Mason, Cork, Hancock, & Dooley, 2013). Other common topical treatments, namely vitamin D analogues and coal tar preparations, can cause skin irritation, and coal tar is particularly messy, has an off-putting smell and can stain skin and clothing (Cohen et al., 2012). Long-term use of ultraviolet-B (UVB) phototherapy leads to premature ageing of the skin and may increase the risk of skin cancer (Menter et al., 2010), and usually involves a disruption in daily/work life due to the need to frequently travel to special facilities to undergo treatment (Cohen et al., 2012). Systemic treatments have numerous potential side effects, some relatively mild, such as dryness of lips, nostrils, eyes, and skin; and headaches, dizziness, fatigue or gastrointestinal complaints (Menter et al., 2009). More severe possible side effects include increased risk of infection, hyperlipidaemia, hypertension, kidney or liver toxicity or reduced function, lung disease and an increased risk of some cancers (Menter et al., 2009). Biologic treatments also increase the risk of infection, and possibly the risk of developing disorders such as multiple sclerosis, liver disease, lupus-like syndromes and some cancers (Menter et al., 2008a). Also, as biologics are relatively new, their safety over the very long-term has yet to be established (Ryan et al., 2014).

Effectiveness, safety and convenience are three of the most important factors relating to treatment satisfaction in people with psoriasis (Van Cranenburgh et al., 2013). Therefore, it follows that many people are dissatisfied with psoriasis treatments, further compounding the burden of living with the condition (Nash et al., 2015). In biannual surveys of the American National Psoriasis Foundation conducted between 2003 and 2013 ($n = 5,604$), 52% of respondents reported treatment dissatisfaction, particularly those with severe psoriasis (Armstrong, Robertson, Wu, Schupp, & Lebwohl, 2013a). Across a sample of 1,564 members of the Psoriasis Association in the UK, coping with treatments was a problem for 44% of respondents, making it one of the most common ways in which psoriasis negatively impacted people's daily lives (Nash et al., 2015). Topical treatments are frequently perceived in a negative light, with many considering them to have low levels of efficacy, as well as being sticky, messy, difficult and time-consuming to apply (Fouere, Adjadj, & Pawin, 2005; Nash et al., 2015). The impact of using topical treatments has been described as "stressful", "difficult to maintain" and "a bigger nuisance than the condition" (Nash et al., 2015, p. 420). Concerns about the potential risks of psoriasis treatments are also common, particularly in relation to systemic and biologic treatments and phototherapy (Van Cranenburgh et al., 2013), with a fear of side effects expressed by over half of participants in a large, multi-national study (Bewley et al., 2014). Furthermore, treatments that lack efficacy alongside the prognosis of psoriasis as a typically interminable condition also contribute to a sense of pessimism and powerlessness, and to overall psychological morbidity (Magin et al., 2009a). Perceptions such as these contribute to low compliance with using treatments as prescribed, and therefore non-compliance is a major issue amongst people with psoriasis (Bewley & Page, 2011). In a study conducted across Europe and the UK ($n = 1,281$), three-quarters of participants reported not complying with their treatment regimes for reasons in line with those described above (Fouere et al., 2005). Non-adherence to available treatments in people with psoriasis is of concern, because many people can in fact significantly improve their psoriasis by following treatment regimens as prescribed (Feldman et al., 2008). It has been proposed that adherence to psoriasis treatments could be improved by, in particular, improving the convenience and issues around cosmetic acceptability

that currently pertain to topical treatments (Bewley & Page, 2011).

Despite the potential risks of biologic therapies, these are associated with the greatest overall satisfaction compared to other psoriasis treatments because of their relatively higher rate of efficacy and convenience of use (Baker et al., 2013; Callis Duffin et al., 2014; Ragnarson Tennvall et al., 2013; Van Cranenburgh et al., 2013). Even so, of the 14% of participants in a recent New Zealand Psoriasis Association survey ($n = 492$) who had used biologic treatments, only 36% found them to be either very or extremely effective (StollzNow Research, 2013). The expense of biologics also prohibits their widespread use; psoriasis patients in New Zealand currently have to meet strict criteria to be eligible for government funding, which includes having psoriasis that has been at severe levels for a minimum of six months, and which has either not responded to any other treatment, or to have had intolerable side effects arising from other treatments (My Psoriasis, 2015). As it is now well established that psoriasis can bring about significant detriment to quality of life even in those with clinically mild disease (Stern et al., 2004), it is important that people with psoriasis at any level of clinical severity are able to access treatments that can safely and effectively ameliorate psoriasis symptoms with minimal accompanying burden, as they are likely to have a correspondingly positive effect on sufferers' lives.

Previous research suggests that potential for psoriasis treatment may be found in oral vitamin D₃ supplements, which are inexpensive and widely available. Keratinocytes and immune cells involved in the pathophysiology of psoriasis possess the vitamin D receptor (VDR), meaning that they have the ability to respond to calcitriol, the hormonally active form of vitamin D (Baeke, Takiishi, Korf, Gysemans, & Mathieu, 2010; Stumpf, Sar, Reid, Tanaka, & DeLuca, 1979). Calcitriol has been shown to reduce skin cell proliferation, normalise differentiation of keratinocytes into the appropriate cell types, and alter the immune response to promote a less inflammatory state, and it is for these reasons that topical analogues of vitamin D have become mainstays in the range of options available to treat psoriasis (Guilhou, 1998). In past decades, there has been interest in whether supra-physiologic doses of oral calcitriol can improve

psoriasis, but results have been inconsistent, and as calcitriol plays a crucial role in the absorption of calcium, managing the risk of elevated calcium levels has been a challenge (Morimoto et al., 1986; Perez, Raab, Chen, Turner, & Holick, 1996; Siddiqui & Al-Khawajah, 1990; Smith, Pincus, Donovan, & Holick, 1988; Takamoto et al., 1986). Yet, keratinocytes and immune cells also possess the necessary enzymes to produce calcitriol intra-cellularly in the presence of adequate calcidiol, its substrate (Baeke et al., 2010), suggesting that raising calcidiol concentrations could be of benefit to psoriasis.

Calcidiol is the major circulating form of vitamin D, and is the best indicator of vitamin D status (Holick et al., 2011). While keratinocytes are known to be able to use locally-produced calcidiol to produce the active form of vitamin D, it remains undetermined whether they are also able to use systemically-circulating calcidiol (i.e., that present in the serum component of the blood) for this purpose, and if so, what the optimum systemic calcidiol concentrations might be to achieve this. Yet, findings from several studies have suggested that there is a significant inverse relationship between serum calcidiol concentrations and severity of psoriasis (Bergler-Czop & Brzezińska-Wcisło, 2016; Chandrashekar et al., 2015; Finamor et al., 2013; Kincse et al., 2015; Osmancevic, Landin-Wilhelmsen, Larko, Wennberg, & Krogstad, 2009a). In general, the optimal level of serum calcidiol is controversial; the Institute of Medicine (IOM) defines vitamin D sufficiency as a concentration of 50 nmol/L (Ross et al., 2011), while others advocate a minimum concentration of 75 to 80 nmol/L for optimal physiological functioning of calcitriol (Glowacki, 2007; Heaney, 2005; Heaney & Holick, 2011; Holick et al., 2011). Most calcidiol is formed through physiological processes that occur following the exposure of skin to UVB in sunlight (Osmancevic, Landin-Wilhelmsen, Larko, & Krogstad, 2010). However, this means vitamin D production can be limited under certain conditions, such as in the wintertime, or if a person spends most of their time indoors or well-covered with clothing. In particular, the latter may apply to those with psoriasis, given that they often keep their skin covered up (Touma et al., 2011). Adequate doses of oral vitamin D₃ are another means by which serum concentrations of calcidiol can be raised (Ilahi, Armas, & Heaney, 2008). Intakes of less than 10,000

International Units (IU) of vitamin D₃ per day are thought to pose little to no risk of toxicity, are inexpensive, easy to administer and widely available (Vieth, 1999). The Endocrine Society (ES) proposes a daily dose of 1000 – 2000 IU for those of normal body weight, or 3000 – 4000 IU for those who are overweight, in order to reach vitamin D levels of at least 75 nmol/L (Holick et al., 2011). As a fat-soluble vitamin, vitamin D₃ can also be taken less frequently as a mega-dose, which is even more convenient than a daily supplement (Kearns, Alvarez, & Tangpricha, 2014).

In a recent open-label pilot study, a very high dose of 35,000 IU per day over 6 months led to significantly increased calcidiol concentrations and significant improvements in psoriasis severity in all 9 participants, with a negative correlation found between Psoriasis Area and Severity Index (PASI) score and serum calcidiol concentrations (Finamor et al., 2013). These participants had to consume a very low calcium diet and be closely monitored for signs of vitamin D toxicity due to the unknown safety profile of such a high dose of vitamin D₃, which are limitations to the widespread use of a dose at this level. Yet, alongside other previously observed associations between serum calcidiol and psoriasis severity (Bergler-Czop & Brzezińska-Wcisło, 2016; Chandrashekar et al., 2015; Kincse et al., 2015; Osmancevic et al., 2009a), the findings of this pilot study support the merit of further investigating the potential of supplemental vitamin D₃ as a psoriasis treatment.

The need for greater understanding of the experience of psoriasis and the need for more safe and convenient treatment options form the basis of the two major, complementary aims of this thesis. The first is to gain a deeper understanding of how people experience living with psoriasis through identifying and analysing the narratives they use to describe their experiences. The majority of previous research into aspects of living with psoriasis has used quantitative methods, with data gathered by way of closed-ended questionnaires covering issues predetermined by the researcher. While this type of research has value in establishing, for example, the prevalence of particular issues, or the degree to which people find these issues to be bothersome, it does not offer any insight into *how* psoriasis is experienced, and the

contextual factors that contribute to their experience. Nor does it offer participants the opportunity to describe the specific experiences of psoriasis that are of most significance to them. On the other hand, a small number of qualitative studies have investigated what it is like to live with psoriasis from the perspective of those who suffer from it, and such research provides some valuable insights into how people experience psoriasis; these studies are discussed in more detail in Chapter 3. Narrative analysis is a type of qualitative inquiry that is based on the premise that people make sense of their world according to underlying narrative forms, and understanding these forms can offer rich insight into what it means for a person to live with the disease (Frank, 2013). As no previous research has yet considered the narrative forms that people use in relation to living with psoriasis, the present research will offer new insights into how people experience the condition. This research is conducted with the overarching hope that awareness about how people are affected by psoriasis can be increased, which is an important goal due to the lack of understanding and stigmatisation that frequently surrounds psoriasis. In addition, the more that healthcare professionals can understand their patients' perspectives of what it is like to live with psoriasis, the better they may be able to provide them with the most effective care (Kennedy, 2006; Kleinman, 1988).

In light of the burden associated with living with psoriasis, the dissatisfaction with available psoriasis treatments and the evidence suggesting a possible relationship between systemic vitamin D levels and psoriasis severity, the second aim of this thesis is to determine whether oral vitamin D₃ supplementation is an effective treatment for psoriasis. This will be assessed by way of a randomised, double-blinded, placebo-controlled trial conducted over a 12-month period, using a monthly mega-dose of 100,000 IU of vitamin D₃ (200,000 IU at baseline). As psoriasis is not usually life-threatening, the significance of identifying whether oral vitamin D₃ can improve psoriasis comes down to how such a treatment might be important for people's lives. Therefore, the deeper understanding of the experience of psoriasis that is sought in the first part of this thesis imbues the second part, aimed at determining whether oral vitamin D₃ is an effective treatment for psoriasis, with greater meaning.

Having now provided a rationale for each study and for the thesis as a whole, the following chapter presents an overview of psoriasis in order to provide context for the two research studies to follow.

2. An Overview of Psoriasis

The purpose of this chapter is to provide an understanding of psoriasis, including its clinical characteristics and proposed co-morbidities, which will provide context for considering how people experience living with the condition in Chapters 3 and 4. Relatedly, it will briefly discuss the aetiology and epidemiology of psoriasis, to indicate who tends to be affected by the condition and the extent of its global prevalence. It will then discuss what is known about psoriasis at a more detailed, cellular level, in order to relate the actions of vitamin D to the processes involved in the development of psoriasis in Chapter 5. Finally, it will conclude with a summary of the treatments that are currently available for psoriasis, which provides context for understanding both the experience of psoriasis and the need for investigation into further treatment options.

2.1. Background and definition

Chronic plaque psoriasis was once thought to be merely a benign skin disorder, as its most obvious manifestation is as raised, reddened, well-demarcated patches covered in flaky scales ('plaques') that appear on various parts of the body (Baker et al., 2016). Yet, in recent years, the understanding of psoriasis has evolved so that it is now seen as a more complex, systemic condition that is associated with numerous other serious diseases, including a unique and debilitating type of arthritis, Crohn's disease, cancer, type 2 diabetes and cardiovascular disease (Baker et al., 2016; Lee, Lin, & Lai, 2014; Myers, Gottlieb, & Mease, 2006; Ogdie et al., 2015; Wu, Nguyen, Poon, & Herrinton, 2012). It has also become appreciated that the implications of psoriasis usually extend far beyond the clinical appearance of skin, to the point where they impact a person's wellbeing and quality of life (Nash et al., 2015). As psoriasis affects between 2% and 5% of the Western world (Parisi et al., 2013), the collective impact of psoriasis is undoubtedly significant. However, treating this disease has long been a source of great frustration for patients and the medical profession alike; as the renowned American dermatologist Bechet expressed eighty years ago: psoriasis is an "antidote for the

dermatologist's ego" (Bechet, 1936, p. 1). This statement is still relevant in the present, because even today, at a time when more is understood about the pathophysiology of psoriasis than ever before, and the range of treatment options has multiplied, many of the complexities of psoriasis are still to be fully unraveled and individual responses to treatments are widely variable (Boehncke & Schön, 2015).

The name 'psoriasis' derives from the Greek *psora*, which means, 'to itch' (Yosipovitch, Goon, Wee, Chan, & Goh, 2000). Historically, however, *psora* did not only refer to psoriasis, but also to a number of unrelated yet clinically similar inflammatory skin conditions that were assumed to be progressions of the same disease (Cowden & Van Voorhees, 2008), and it was not until the mid-19th century that psoriasis was defined as a distinct entity (Schön & Boehncke, 2005). To this day, however, a precise definition of psoriasis is still lacking. It is widely referred to as one of the immune-mediated inflammatory conditions, a group of diseases without a definitive aetiology that also includes Crohn's disease, rheumatoid arthritis and ankylosing spondylitis (Vangeli et al., 2015), although some of these have also been described as autoimmune diseases (Wu et al., 2012). Similarly, psoriasis has also been classified as an autoimmune disease (Raychaudhuri, Maverakis, & Raychaudhuri, 2014), that is, a disease that occurs when the immune system mistakenly recognises normal cells and tissues as being foreign to the body (i.e., as 'antigens') and mounts an immune response against them.

Also lacking is clear diagnostic criteria for psoriasis, and the term currently covers a wide spectrum of presentations (Raychaudhuri et al., 2014). Within this spectrum are a number of types of psoriasis, including chronic plaque, guttate, erythrodermic, palmoplantar and pustular psoriasis, of which chronic plaque psoriasis, or *psoriasis vulgaris*, is by far the most common, affecting around 90% of those with psoriasis (Griffiths & Barker, 2007). Guttate psoriasis appears as scaly, teardrop-shaped spots, and often develops in children and adolescents after a streptococcal or upper respiratory tract infection, and those who have had guttate psoriasis are more likely to develop plaque psoriasis (Raychaudhuri et al., 2014). Palmoplantar psoriasis affects the palms of the hands and/or the soles of the feet, and pustular psoriasis involves the

development of non-infectious, pus-filled blisters, and both can be present alongside plaque psoriasis (Boehncke & Schön, 2015; Raychaudhuri et al., 2014). Erythrodermic psoriasis is a potentially life-threatening complication that can occur in rare cases of psoriasis, with the estimated prevalence amongst people with psoriasis ranging from 1% to 2.25% (Stinco & Errichetti, 2015). It involves generalised inflammation across the majority of the skin's surface area, and while the aetiology of erythrodermic psoriasis is not understood, possible triggers include systemic illness, emotional stress, sudden withdrawal of psoriasis treatments, ultraviolet burns and alcoholism (Stinco & Errichetti, 2015). As this thesis is focused on chronic plaque psoriasis, other types of psoriasis will not be discussed further in this review unless relevant to plaque psoriasis.

2.2. Clinical features and sub-classifications

Psoriasis is characterised by and diagnosed according to its clinical appearance. The classic presentation of psoriasis is distinctive: patches or plaques appear on the skin as well-demarcated, raised, inflamed lesions covered in silvery-white flaky scales (**Figure 1A**). Psoriatic lesions can appear anywhere on the body, with the elbows, knees, lumbar and umbilicus area and/or scalp the most commonly affected sites (Griffiths & Barker, 2007) (**Figure 1B, 1C**). They often appear in symmetrical and bilateral fashion, that is, opposing sides of the body may have plaques that are near mirror images of each other (Figure 1C) (Luba & Stulberg, 2006). Plaques exhibit pin-prick bleeding upon removal of scales, which is known as the Auspitz sign, and occurs due to the proximity of dilated capillaries to the surface of the skin (Raychaudhuri et al., 2014). Around 20% of psoriasis patients experience the Koebner phenomenon, which is the development of new psoriatic plaques on skin following irritation or trauma (Myers et al., 2006). Other common symptoms of psoriasis are itch, and skin that is painful, burning, stinging, sensitive, cracked and bleeding (Globe, Bayliss & Harrison, 2009). The visible manifestations of psoriasis can also extend to the nails, with an estimated 80% – 90% of people with psoriasis developing nail disease (onychodystrophy) during their lifetime (**Figure 1D**) (Reich, 2009). This tends to affect fingernails more often than toenails, and takes

the form of pitting, separation of the nail plate from the nail bed (onycholysis), yellow or brown marks caused by an accumulation of cellular debris under the nail (known as oil spots) and/or nail dystrophy (Griffiths & Barker, 2007).



Figure 1. The clinical appearance of psoriasis¹

(A) Characteristic silvery-white flaky scale on a psoriasis plaque; (B) and (C) the elbows and knees are typical sites of psoriasis development. Figure (C) shows symmetrical and bilateral plaque development. (D) Onychodystrophy (nail disease) in psoriasis: nail pitting and onycholysis (separation of the nail from the nail bed); (E) flexural psoriasis occurs in skin folds and has a shiny appearance without scales.

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While the aforementioned features are considered ‘classic’ features of psoriasis, in practice the term encompasses a variety of presentations. For instance, the size, thickness and type of lesion (macule, papule or plaque) can vary greatly between, or even within, individuals (Raychaudhuri et al., 2014). For some, psoriasis is widespread across the body, whereas for others it is localised to one particular region (Raychaudhuri et al., 2014). Similarly, the site of plaque development can vary, as can the pattern of distribution; for example, a sub-type called flexural

psoriasis occurs only within skin folds and is without scales (**Figure 1E**), whereas another subtype, sebopsoriasis, tends to develop on the face, behind the ears and on the sternum, and scales are greasy and yellow (Griffiths & Barker, 2007). Furthermore, the severity of psoriasis ranges from mild to severe based on the degree of visible inflammation, thickness and scaling (Schmitt & Wozel, 2005).

A further point of variation amongst those with psoriasis is the age at which psoriasis first develops. Age of onset, like much of the condition, is unpredictable, and can occur anytime between infancy and old age (Naldi & Gambini, 2007). However, Henseler and Christophers noted a bimodal pattern of age of onset, with the first peak occurring between 16 and 22 years and the second between 57 and 60 years (as cited in Griffiths & Barker, 2007). Early onset of psoriasis (< 40 years) is much more common than late onset (Naldi & Gambini, 2007) and women are thought to develop it slightly earlier than men (Griffiths & Barker, 2007). Further investigation in this area has identified clinical and genetic differences between those who develop psoriasis early in life (defined as onset < 40 years) compared to those who develop it later (> 40 years), leading to the concepts of Type I and Type II psoriasis, which describe early and late onset psoriasis, respectively (Naldi & Gambini, 2007). Those with Type I psoriasis, which is more common, are thought to be more likely to have severe, recurrent disease, more frequent nail disease, and to have at least one first-degree relative with psoriasis, compared to those with Type II psoriasis, which tends to be a milder, more stable condition and in which the suggestion of heredity is not as clear (Naldi & Gambini, 2007). However, age of onset does not appear to be a reliable indicator of psoriasis characteristics in its own right, as these associations are not consistently found (Guinot, Latreille, Perrussel, Doss, & Dubertret, 2009).

In one of the more comprehensive explorations into the distinctions between phenotypes of psoriasis, Guinot et al. (2009) also proposed six different phenotypes based on observed clusters of self-reported clinical characteristics, including age of onset and severity, in 1,484 participants. The most common of these were Type 1, which involved late onset development, few lesions involving mainly the scalp and elbows, no associated arthritis, continuous

development and no apparent family history or sensitivity to environmental factors; and Type 4, which involved very severe psoriasis affecting all areas of the body except soles of feet, palms of hands and nails, no association with age of onset, lower sensitivity to the Koebner phenomenon, and less association with itch as a symptom, and with personal and family history of arthritis, atopic dermatitis, asthma or allergic rhinitis (Guinot et al., 2009). While still unlikely to be definitive, these findings illustrate the large variability that is found between forms of the disease that are currently classified as psoriasis. Due to this variety in the presentation and occurrence of psoriasis, it has been proposed that what is currently defined as chronic plaque psoriasis is actually a number of closely related, but geno- and phenotypically distinct conditions (Griffiths & Barker, 2007). At the very least, psoriasis may be best thought of as a spectrum of disease rather than a clearly delineated disease entity (Raychaudhuri et al., 2014). A summary of ways in which psoriasis has been sub-classified is presented in **Table 1**. Some of these classifications have been developed in an attempt to explain the significant variation in course and response to treatment that exists amongst people with psoriasis, and as these attempts have usually focused on one binary pair (e.g., thick vs. thin plaque psoriasis, Type I vs. Type II psoriasis), significant overlap exists between classifications.

2.3. Co-morbidities

Alongside its skin manifestations and contributing to its reconceptualisation as a systemic disease, people with psoriasis are thought to be more susceptible to the development of a number of significant co-morbidities, including other immune-mediated inflammatory diseases, cardiometabolic diseases, autoimmune diseases, cancers, non-alcoholic fatty liver disease and psychiatric disorders (Ni & Chiu, 2014). It has been estimated that 73% of people with psoriasis have at least one co-morbidity (Machado-Pinto, Diniz, & Bavoso, 2016), and overall, people with severe psoriasis have a life expectancy six years less than those without psoriasis (Abuabara et al., 2010), contributing to the burden of disease.

Table 1. Sub-classifications of plaque psoriasis¹

Classification criteria	Name or description	Clinical phenotype
Plaque thickness ²	Thick plaque psoriasis	≥ 1.0 mm thick
	Thin plaque psoriasis	< 0.05 mm thick
Age of onset ³	Type I psoriasis	Onset < 40 years
	Type II psoriasis	Onset > 40 years
Severity ⁴	Mild psoriasis	PASI < 7 or < 5% BSA
	Moderate psoriasis	PASI 7 – 12 or 5 – 10% BSA
	Severe psoriasis	PASI > 12 or > 10% BSA
Pattern of distribution ⁵	Localised psoriasis	Plaques are few, may be scattered over different parts of body
	Widespread psoriasis	Plaques cover large areas of skin
Site of development ⁵	Flexural (inverse)	Occurs within skinfolds (armpits, groin, under breasts, between buttocks). Appears shiny, red and without scale.
	Sebopsoriasis	Psoriasis and seborrhoeic dermatitis occur simultaneously. Affects the face, behind the ears and on the sternum. Appears greasy with yellow scales.
	Scalp psoriasis	Occurs on the scalp.
	Palmoplantar psoriasis	Affects palms of hands and/or soles of feet.
	Genital psoriasis	Occurs on the genital area.
	Nail psoriasis	Appears as pitting, oil spots and onycholysis.

Continued on next page

Type 1	Late onset; few lesions involving mainly the scalp and elbows; no associated arthritis; continuous evolution; no sensitivity to environmental factors or family antecedents.
Type 2	Large plaques involving the palms of hands and/or soles of feet; pustules common; associated arthritis; commonly experience contact dermatitis.
Type 3	Early onset; few body sites involved; sensitivity to environmental factors; associated with guttate psoriasis; personal and family history of psoriasis, arthritis and/or dermatitis/asthma/allergic rhinitis; often improves with exposure to sun and sea.
Type 4	Very severe psoriasis affecting any areas of the body except soles, palms and nails; not linked to age of onset; low sensitivity to Koebner phenomenon; less association with itch, and with personal and family history of arthritis and dermatitis/asthma/allergic rhinitis.
Type 5	Early onset; widespread lesions, sensitivity to environmental factors; personal and family history of psoriasis, arthritis and dermatitis/asthma/allergic rhinitis; often improves with exposure to sun and sea.
Type 6	Large plaques affecting all body sites including soles and palms; strong association with metabolic syndrome; itch and sensitivity to environmental factors are common.

Cluster of clinical characteristics⁶

PASI, Psoriasis Area and Severity Index; BSA, body surface area

¹Overlap exists between classifications

²Rakkhit et al. (2009)

³Henseler & Christophers (1985), as cited in Griffiths & Barker (2007)

⁴Schmitt & Wozel (2005)

⁵Boehneke & Schön (2015)

⁶Guinot et al. (2009)

Of the proposed co-morbidities, the strongest association is between psoriasis and psoriatic arthritis, an immune-mediated inflammatory arthritis that can cause physical disability, pain and significant reduction in quality of life (Myers et al., 2006). In the wider population, psoriatic arthritis has an estimated prevalence of 0.25%, whereas in those with psoriasis, reported prevalence ranges from 6% to 42% (Gladman et al., 2005). Damage to joints is usually permanent, and leads to reduced joint function and higher mortality rates, as well as affecting a person's social relationships and their capacity to work (Myers et al., 2006).

In 75% to 85% of cases, psoriatic arthritis develops after the onset of psoriasis, with an average lag of 10 years, and in the remainder, it either develops at the same time or occasionally prior to skin lesions (Myers et al., 2006). Psoriasis and psoriatic arthritis are linked through a shared genetic background, and there are strong similarities in the cellular and inflammatory cytokine patterns in the joints in arthritis and in the skin in psoriasis (Myers et al., 2006).

Evidence is also accumulating for a relationship between psoriasis and cardiovascular disease (Miller, Ellervik, Yazdanyar, & Jemec, 2013) and its numerous risk factors, such as type 2 diabetes (Azfar et al., 2012; Lee et al., 2014), hypertension (Cohen, Weitzman, & Dreiherr, 2010; Miller et al., 2013), obesity and metabolic syndrome (Miller et al., 2013) and dyslipidaemia (Ma, Harskamp, Armstrong, & Armstrong, 2013; Miller et al., 2013). Psoriasis has also been associated with increased overall mortality risk (Prodanovich et al., 2009), and cardiovascular disease has been shown to significantly contribute to the reduced life span predicted for those with moderate-to-severe psoriasis (Abuabara et al., 2010). While some research has found an association between mild psoriasis and cardiovascular disease (Armstrong, Harskamp, & Armstrong, 2013b), the strongest associations have been found in those with moderate-to-severe psoriasis (Miller et al., 2013), and the risk of cardiometabolic co-morbidities seems to increase with psoriasis severity (Ogdie et al., 2015; Yeung et al., 2013a).

People with psoriasis also seem to have a higher likelihood of having an autoimmune disease compared to the wider population. In a retrospective cohort study of 25,341 psoriasis patients

and five matched controls per person, the odds ratio (OR) of having an autoimmune disease was 1.6 (95% CI 1.5 – 1.7) for those with psoriasis compared to those in the general population, and the odds of having two autoimmune diseases was even higher (OR 1.9; 95% CI 1.6 – 2.4) (Wu et al., 2012). In this same analysis, psoriasis was significantly associated with 14 of 17 predetermined autoimmune diseases, including rheumatoid arthritis, celiac disease, Crohn's disease, vitiligo, ulcerative colitis and systemic lupus erythematosus (Wu et al., 2012). Furthermore, a number of psychiatric disorders have been associated with psoriasis, including depression, anxiety, schizophrenia, sleep disorders, eating disorders and substance dependence/abuse (Biljan, Laufer, Filaković, Šitum, & Brataljenović, 2009; Ferreira, Da Costa Abreu, Dos Reis, & Da Costa Figueiredo, 2016). Conditions such as depression, anxiety and substance abuse may result from having psoriasis, or may trigger or worsen psoriasis, or both (Ferreira et al., 2016).

The underlying mechanisms linking psoriasis with each of these co-morbidities are not fully understood, but it is hypothesised that the primary physiological link between psoriasis and cardiovascular diseases, non-alcoholic fatty liver disease, cancers, autoimmune diseases and perhaps even depression may be a chronic state of inflammation (Armstrong et al., 2013b; Ni & Chiu, 2014; Parisi et al., 2015). Higher serum levels of some pro-inflammatory cytokines, as well as C-reactive protein (CRP), a marker of systemic inflammation, have been observed in the psoriatic population ($n = 3,085$) compared to healthy controls ($n = 4,767$) (Dowlatshahi, Van Der Voort, Arends, & Nijsten, 2013). It remains unknown whether the inflammatory state in psoriasis contributes to the development of co-morbidities, or *vice versa* (Dowlatshahi et al., 2013). It is also likely that genetic factors link psoriasis with co-morbid diseases, particularly autoimmune and immune-mediated inflammatory diseases, as they share common genetic loci (Wu et al., 2012). However, the genetic complexity of these conditions precludes the relationship from being quickly understood. Other factors that may also contribute to increased risk of co-morbidities in psoriasis are shared lifestyle factors such as excess alcohol intake, which is more prevalent in those with psoriasis than in healthy controls, and smoking, which is

associated with increased risk of psoriasis onset and exacerbation (Hayes & Koo, 2010). In sum, a higher prevalence of numerous other serious diseases occurs in the psoriatic population compared to those without psoriasis, some of which share a common genetic background with psoriasis, and others potentially linked with psoriasis through an underlying state of systemic inflammation.

2.4. Epidemiology

Globally, psoriasis is one of the most common skin disorders, but the prevalence of psoriasis differs considerably between geographic locations and ethnicities. A systematic review of 46 prevalence studies covering 21 countries at various latitudes showed that the majority had a psoriasis prevalence of between 2.2% and 5.2% amongst adults (Parisi et al., 2013). However, prevalence has been reported to be as low as no cases in Samoa, and as high as 11.8% in the Arctic Kasach'ye (Jacobson, Kumar, & Kimball, 2011). Across all ethnicities, psoriasis is most common in Caucasian populations (Griffiths & Barker, 2007). There may be an association between prevalence and latitude, as it has been proposed that psoriasis is found more frequently in locations further from the equator compared to those closer to it (Parisi et al., 2013).

There does not appear to be any official psoriasis prevalence data for the New Zealand population. In Australia, its closest neighbour, estimates have ranged from 2.3% (95% CI 1.39 – 3.21) to 6.6% (95% CI 5.4 – 7.9) (Parisi et al., 2013). The true prevalence of psoriasis may not be accurately reflected in reported figures because of the lack of validated diagnostic criteria for psoriasis (Griffiths & Barker, 2007), because data has been based on self-reported as well as clinically diagnosed psoriasis (Parisi et al., 2013), and because reported prevalence probably excludes people who do not seek treatment. Further, reported prevalence has been defined as occurring over a lifetime, a set period, or at one point in time (Parisi et al., 2013), the choice of which may affect the results. Therefore, a prevalence of 2% to 5% probably represents a minimal estimate of the global prevalence of psoriasis.

2.5. Aetiology

Considerable effort has been made to determine the causes of psoriasis, yet a complete, conclusive understanding has remained elusive (Ryan et al., 2014). Evidence to date suggests that psoriasis manifests in people who are genetically predisposed and also exposed to particular environmental triggers (Mahajan & Handa, 2013).

2.5.1. Genetic factors

Strong evidence supports the heritability of psoriasis, which has been estimated at 60 – 90% (Elder et al., 2001). There is a higher prevalence of psoriasis among those who have a first-degree relative with the disease than those who do not (Perera, Di Meglio, & Nestle, 2012). Psoriasis occurs in as many as half of the siblings of a person with psoriasis when both parents are also affected; when only one parent has psoriasis, prevalence falls to 16%, and when neither parent is affected, it is 8% (Schön & Boehncke, 2005). Furthermore, a number of studies also show significantly greater concordance in monozygotic (between 35% and 73%) than dizygotic twins (12 – 20%) (Lønnberg et al., 2013). However, these studies also highlight the fact that genes are not the only important factor in the development of psoriasis. For instance, in the largest twin study in psoriasis to date (10,725 twin pairs), genetic factors explained just 68% of the variation in the susceptibility to psoriasis (Lønnberg et al., 2013).

While the case for heredity has been established, identifying the genes predisposing a person to psoriasis has proved to be a complex and challenging task. Except in rare cases, in which inheritance of psoriasis follows a Mendelian pattern (the passing on of a single gene), inheritance of psoriasis appears to involve multiple genes (Barker, 2014; Nestle, Kaplan, & Barker, 2009). At least 41 susceptibility loci for psoriasis have been identified (Tsoi et al., 2015), however, it has been estimated that current knowledge only accounts for 30% of the genetic basis of psoriasis (Barker, 2014). The genetic loci that have been identified as being associated with psoriasis tend to harbour genes involved in the innate and adaptive immune systems and in skin barrier function, supporting the central role of these aspects in the

pathogenesis of psoriasis (Mahil, Capon, & Barker, 2015).

Psoriasis susceptibility locus 1 (*PSORS1*) is the major known genetic determinant of psoriasis, associated with up to 60% of psoriasis cases (Perera et al., 2012). People who carry the allele known as HLA-Cw0602* (related to *PSORS1*) have a 20-fold increased risk of developing psoriasis, and 10% to 15% of the general population carry this allele (Perera et al., 2012). Yet, only about 10% of people who have the allele develop psoriasis, therefore many people carry alleles of psoriasis susceptibility but never get the disease (Jullien & Barker, 2006). In such cases, it must therefore be that other genetic factors and/or environmental triggers are lacking.

2.5.2. Environmental triggers

Increased risk of both onset and severity of psoriasis has been associated with a range of environmental factors, namely high body weight and smoking (Wolk et al., 2009), certain medications (lithium, beta-blockers, antimalarials, non-steroidal anti-inflammatory drugs [NSAIDs], tetracyclines and oral steroid withdrawal), physical trauma, including tattoos (which can trigger the Koebner phenomenon) and alcohol intake (Perera et al., 2012). Streptococcal infection is a common precursor of guttate psoriasis, which in turn can trigger plaque psoriasis (Naldi & Gambini, 2007). Human immunodeficiency virus tends to elicit severe exacerbations of psoriasis (Luba & Stulberg, 2006). Psychological stress is also thought to play a role in the onset and exacerbation of psoriasis (Devrimci-Ozguven, Kundakci, Kumbasar, & Boyvat, 2000). For many, there is a seasonal influence, with psoriasis worsening in the winter and improving in summer, although the reverse is sometimes the case (Naldi & Gambini, 2007).

2.6. Processes involved in plaque formation

Formation of psoriatic plaques is a result of a number of adverse changes occurring at the histopathological (tissue) and pathophysiological (physiological process) level in affected skin. The epidermis is the outermost layer of skin, and keratinocytes are the predominant cell type in the epidermis (Gniadecki, 1998). The primary differences between psoriatic and normal skin

are a greatly increased rate of keratinocyte proliferation, keratinocytes that fail to differentiate into the appropriate cell type, increased angiogenesis (formation of new blood vessels) and an infiltrate of immune cells into the epidermal and dermal layers of the skin (Chong, Kopecki, & Cowin, 2013; Schön & Boehncke, 2005). These abnormal processes only occur in the regions where psoriatic lesions develop (**Figure 2**) (Schön & Boehncke, 2005).

Hyperproliferation of keratinocytes occurs as cell division takes place at a rate that is 8-fold that of normal skin (Weinstein, McCullough, & Ross, 1984). Additionally, cells take just three to five days to traverse from the basal layer of the epidermis to the outermost layer, the *stratum corneum*, compared to the usual 28 to 30 days (Schön & Boehncke, 2005). Further, apoptosis, or programmed cell death, is decreased in psoriasis (Kaštelan, Prpić-Massari, & Brajac, 2009), and the result of these factors is a large imbalance between the generation of new skin cells and the sloughing of old cells, leading to the characteristic flaky scale and a marked increase in the number of epidermal cells. As a consequence, the epidermis becomes thickened, with elongated, ‘finger-like’ projections (‘rete ridges’) that extend downwards between dermal papillae, and it can also lead to thickening of the *stratum corneum* (Boehncke & Schön, 2015). This process also explains why new scales can reappear on plaques within 24 hours of removal (Camisa, 2004).

Keratinocytes in psoriatic skin also undergo abnormal differentiation, a process that should normally result in a skin barrier that not only physically protects underlying physiological structures, but also protects the body against invasion from pathogens (Proksch, Brandner, & Jensen, 2008). In psoriatic skin, basal keratinocytes fail to properly differentiate, resulting in an incomplete or absent *stratum granulosum* layer in the epidermis (Schön & Boehncke, 2005). In normal skin, this layer is the location at which cells begin to terminally differentiate, with the ultimate goal of becoming one of the outermost skin cells within the *stratum corneum* – effectively ‘dead’ cells lacking a nucleus that form the body’s protective layer. Without the granular layer, keratinocytes progress to the *stratum corneum* with their nuclei still intact,

resulting in abnormal keratinisation (Schön & Boehncke, 2005), and thus, to reduced integrity of the skin barrier.

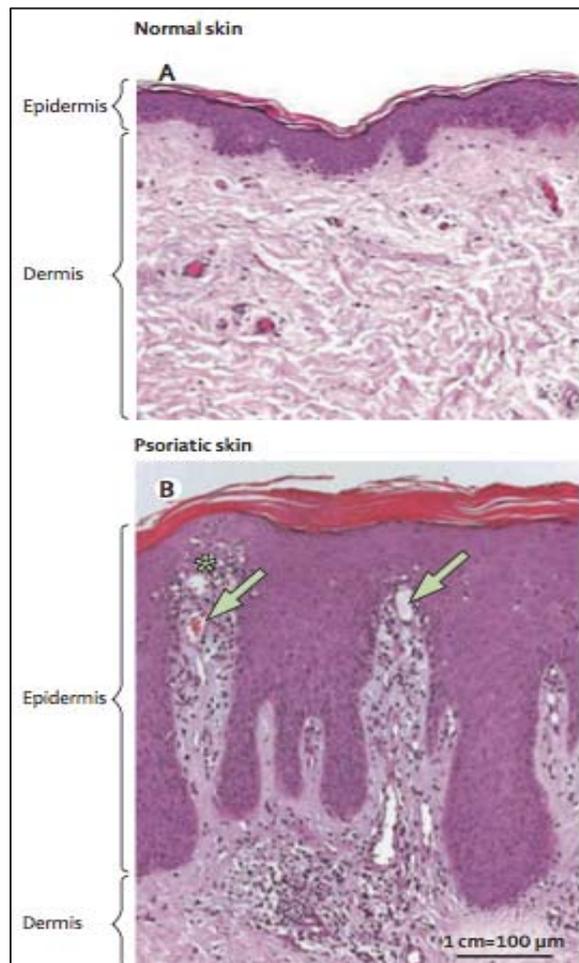


Figure 2. Histopathological features of psoriasis¹

Compared to normal skin (A), psoriatic plaques typically show thickening of the epidermis, the stratum corneum and elongated rete ridges. An inflammatory infiltrate can be seen in the epidermis (asterisk). In the dermis, dilated, elongated and tortuous blood vessels reach into the tips of the dermal papillae (B, arrows).

¹Images reprinted from The Lancet, Vol. 386, Boehncke & Schön, *Psoriasis*, 983-94, Copyright (2015), with permission from Elsevier.

The other major pathophysiological changes in psoriatic skin are increased angiogenesis in the dermis and an infiltration of immune cells into the epidermis and dermis (Chong et al., 2013; Schön & Boehncke, 2005). Angiogenesis leads to increased vascularisation of the dermis, with elongated, dilated and tortuous capillaries in dermal papillae that reach directly beneath the epidermis (Heidenreich, Rocken, & Ghoreschi, 2009). The epidermis and dermis are infiltrated with a number of types of white blood cells, including neutrophils, activated T-cells, macrophages and dendritic cells (Monteleone, Pallone, MacDonald, Chimenti, & Costanzo, 2011), and neutrophils can also accumulate in the *stratum corneum* or the upper *stratum spinosum* layers of the skin (Berth-Jones, 2013).

2.7. Role of the immune system

While not completely understood, a variety of complex interactions is thought to occur between the innate and adaptive immune systems and skin cells to promote the formation of psoriatic plaques (Boehncke & Schön, 2015). The putative series of immune processes leading to the development of psoriatic plaques begins with an environmental trigger, perhaps physical trauma or bacteria, in genetically susceptible people (Boehncke & Schön, 2015; Nestle et al., 2009). This leads to the formation of a complex of DNA and cathelicidin, an antimicrobial peptide that is present in the epidermis and part of the innate immune system, the body's first response mechanism against harm (Nestle et al., 2009). This complex stimulates cells called plasmacytoid dendritic cells to produce the innate cytokine interferon (IFN)- α , leading to the activation of myeloid dendritic cells (Nestle et al., 2005). These activated dendritic cells produce the cytokines interleukin (IL)-12 and IL-23 and present antigens (substances that the body recognises as foreign) to T-cells, which are central to the adaptive immune response. This process causes T-cells to become activated and to mount an immune response to defend against that antigen (Monteleone et al., 2011). The immune response following activation of T-cells involves the production and activation of a range of cytokines and chemokines, with the specific response pathways that are activated dependent on the types of T-helper (Th) cells that the T-cells differentiate into (Monteleone et al., 2011). In psoriasis, these are cells of the Th1 and Th17 pathways (Boehncke & Schön, 2015), which trigger production of pro-inflammatory cytokines such as tumour necrosis factor (TNF)- α , IFN- γ , IL-17 and IL-22; these particular cytokines have been strongly implicated in the development of psoriasis, with elevated levels found in psoriatic plaques (Monteleone et al., 2011). Activated dendritic cells also produce IL-23, which sustains the continued differentiation of Th17 cells and therefore the inflammatory state, and recent research has suggested this 'IL-23/Th17 axis' is also a central factor in the development of psoriasis (Boehncke & Schön, 2015; Coimbra, Figueiredo, Castro, Rocha-Pereira, & Santos-Silva, 2012). T-cells are therefore considered to be central mediators in the development of psoriatic plaques; they make up the majority of the infiltrate of white blood

cells in plaques, and this infiltration precedes the overgrowth of skin cells in the epidermis (Coimbra et al., 2012).

One of the pro-inflammatory cytokines in particular, TNF- α , is also thought to play a central role in the development of psoriasis (Nestle et al., 2009). It is produced by a large range of cell types, including T-cells and keratinocytes, and amplifies the immune response through numerous pathways (Boehncke & Schön, 2015). The importance of TNF- α in the development of psoriasis is illustrated by the success of anti-TNF- α biologic therapies in treating the disease (Grine, Dejager, Libert, & Vandenbroucke, 2015).

As a result of the inflammatory state produced through activation of these inflammatory pathways, almost every type of skin cell enters a state of dysregulation, which promotes the abnormal cellular processes that produce psoriatic plaques (Boehncke & Schön, 2015). For example, IFN- γ , IL-17 and other cytokines stimulate keratinocyte proliferation and other hallmark features of psoriasis (Boehncke & Schön, 2015; Coimbra et al., 2012; Fierlbeck & Rassner, 1990). Keratinocytes that have been activated by cytokines also then produce more antimicrobial peptides, cytokines and chemokines, which contribute to the recruitment and activation of T-cells and antigen-presenting cells in plaques (Nestle et al., 2009). This forms a positive feedback loop between the activation of immune cells and keratinocytes (Boehncke & Schön, 2015). On the contrary, cells that would typically help to maintain homeostasis, such as IL-10 and regulatory T-cells (Treg), appear to either be at reduced levels in psoriasis (Nestle et al., 2009), or in the case of Treg, to have decreased functional ability to suppress the actions of pro-inflammatory cells, perhaps related to a reduced ability to proliferate (Sugiyama et al., 2005).

While an understanding of the histopathological and pathophysiological changes in psoriasis has considerably increased over recent years, less is known about the processes triggering these pathological changes. One of the most recent hypotheses is based on the relationship observed between psoriasis and Crohn's disease, which stems from a breakdown of immune tolerance to

bacteria in the intestine (Mattozzi, Richetta, Cantisani, MacAluso, & Calvieri, 2012). As people with psoriasis share some mutations in innate immunity genes with people with Crohn's disease, it is possible that psoriasis is triggered by a similarly abnormal immune response to bacteria in the skin (Mattozzi et al., 2012).

2.8. Treatments

There is a range of treatments available for psoriasis, which can be categorised according to four different modalities: topical applications, UVB phototherapy, conventional systemic treatments and biologic therapies. Each of these types of treatments has advantages but also disadvantages, ranging from the inconvenience of applying topical treatment to the increased risk of infection and malignancies with systemic and biologic treatments (Bewley et al., 2014; Menter et al., 2008a; Menter et al., 2008b; Nash et al., 2015). As mentioned in Chapter 1, compliance with using treatments as prescribed can be an issue, particularly with the use of topical treatments (Chan, Hussain, Lawson, & Ormerod, 2013). There is also no 'one size fits all' approach, as no treatment is effective in all people (Boehncke & Schön, 2015). The type of treatment a person uses is primarily determined by the severity of their psoriasis, the ability of the person to tolerate the treatment and the efficacy of the treatment for that person (Nast et al., 2012). It is often the case that several treatments may need to be tried before one is found that brings about some improvement, and in many individual cases, no treatments can adequately control the condition. It is well accepted that as there is no cure for psoriasis, there is no permanent solution (Van Cranenburgh et al., 2013). The advent of biologic treatments in recent years has made the prospect of achieving full clearance of skin more possible, but there is limited access to these treatments and even with them, complete clearance is not always achieved (Strober et al., 2016). A more realistic goal for most people with psoriasis is to manage the condition, rather than to clear it completely (Al-Suwaidan & Feldman, 2000; Van Cranenburgh et al., 2013). Specific treatment types will now be discussed, with their characteristics summarised in **Table 2**.

Table 2. Treatments available for chronic plaque psoriasis in New Zealand¹

Treatment	Mechanism	Indication	Treatment efficacy	Advantages	Disadvantages
<i>Topical treatments</i>					
Emollient	Keeps area moisturised	Any psoriasis	-	Lifts scale and reduces cracking; safe	No major disadvantages
Corticosteroids (low potency e.g., hydrocortisone, clobetasone butyrate; high potency e.g., betamethasone valerate/dipropionate, mometasone, clobetasol propionate)	Reduces inflammation	Low potency: on psoriasis on sensitive areas (i.e., face, flexures, genitalia) High potency: on thick-skinned sites (i.e., palms, soles, scalp)	High potency: 62 – 78% achieved PASI 75 in 2 – 4 weeks ²	Low potency: no to minimal irritation High potency: effective even in areas of poor absorption	Constant treatment required; atrophy with long-term use; tachyphylaxis; risk of rebound on withdrawal (high potency); risk of adrenal suppression if long-term use on large area (high potency); risk of cataracts and glaucoma if used on eyelids (low potency)
Vitamin D analogues (calcipotriol)	Normalises keratinocyte differentiation and proliferation	Most psoriasis	54% achieved PASI 75 after 4 weeks ²	Generally well-tolerated	Can cause irritation, especially in flexures; tachyphylaxis
Vitamin D analogue + corticosteroid (calcipotriol + betamethasone dipropionate)	Normalises keratinocyte differentiation and proliferation and reduces inflammation	Most psoriasis	71% achieved PASI 75 after 4 weeks ²	Generally well-tolerated	Can cause irritation, especially in flexures; tachyphylaxis
Coal tar	Reduces scale and itch	Any psoriasis	55% achieved PASI 75 after 4 weeks ²	Generally safe	Offensive smell; stains skin and clothing; long contact time required; can cause irritation at high concentrations; folliculitis; photosensitivity (rare)

Continued on next page

Salicylic acid	Reduces scale	Most useful for thickened areas of psoriasis	3% achieved complete clearance when used alone, 84% achieved when used with topical steroids ³	Reduces scaling to allow other treatments to penetrate skin	Irritating to unaffected skin
Retinoid	Normalises keratinocyte differentiation and proliferation, reduces inflammation	Any psoriasis	27% achieved PASI 75 after 2 – 4 weeks (comparable efficacy to placebo) ²	-	Limited efficacy; irritation; photosensitivity; teratogenic
Dithranol	Reduces keratinocyte proliferation	Large plaques	43% achieved PASI 75 after 4 weeks ²	Effective on thick plaques	Severely irritating to unaffected skin; stains skin and clothing; potential carcinogen
<i>Other treatments</i>					
UVB phototherapy (broadband or narrowband)	Not well understood, but suppresses immune response, pro-apoptotic	Moderate to severe, or recalcitrant psoriasis	Broadband: 59% (95% CI 57, 78) achieved complete clearance between 4 and 24 weeks; narrowband: 68% (95% CI 44, 72) achieved complete clearance between 4 and 24 weeks ⁴	Higher rate of efficacy than topical treatments; minimal side effects	Potential for sunburn; premature ageing of skin and possible increased risk of skin cancers with long-term exposure; inconvenient
Conventional systemic therapies (i.e., methotrexate, ciclosporin, acitretin)	Suppresses immune response	Moderate to severe, or recalcitrant psoriasis	27% (acitretin), 46% (ciclosporin), 40 – 49% (methotrexate) achieved PASI 75 at 12 weeks ⁵	Higher rate of efficacy than topical treatments	Risk of infection and malignancies; and liver (methotrexate, acitretin) and/or kidney damage (ciclosporin); suppressed bone marrow (methotrexate); teratogenic and risk of dyslipidaemia (acitretin)

Continued on next page

Biologic therapies (i.e., adalimumab, etanercept, infliximab, ustekinumab, secukinumab)	Suppresses specific pro-inflammatory cytokines involved in psoriasis pathogenesis	Moderate to severe, or recalcitrant psoriasis, or if adverse effects from other treatments	27 – 68% (adalimumab), 12 – 66% (etanercept), 38 – 53% (infliximab), 63 – 80% (ustekinumab) achieved PASI 75 at 12 weeks ⁵ ; probability of PASI 75 compared to placebo 12.0 (95% CI 8.8, 16.2) (secukinumab) ⁶	Highest rate of efficacy of psoriasis treatments Risk of infection and malignancies, very expensive
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PASI, Psoriasis Area and Severity Index; PASI 75, 75% reduction in PASI score; UVB, ultraviolet-B

¹Table adapted with permission from S. N. Cohen, S. E. Baron, C. B. Archer, *Clinical and Experimental Dermatology*, John Wiley and Sons. © 2012 The Authors.

²Samarasekera et al. (2013)

³Shokeen et al. (2014)

⁴Almutawa et al. (2013)

⁵Zweegers et al. (2016)

⁶Nast et al. (2015)

2.8.1. Topical treatments

Topical applications are used for the treatment of mild-to-moderate psoriasis, which affects approximately 80% of people with psoriasis (Oquendo, Abramovits, & Morrell, 2012). The most commonly used topical treatments are corticosteroids and vitamin D analogues (Segaert & Duvold, 2006), but coal-based preparations, dithranol, salicylic acid and topical retinoids are also available. Also, because psoriasis is a condition of dry skin, temporary relief can often be gained through use of a non-pharmaceutical emollient (moisturiser) (Cohen et al., 2012).

Corticosteroids

The first-line topical treatment is usually a corticosteroid cream, ointment, lotion or gel (Menter et al., 2008b). Corticosteroids are well known for their anti-inflammatory properties, and they can visibly reduce redness and scaling (Menter et al., 2008b). They are divided into four classes according to their strength. Class 4 includes steroids of mild strength, such as hydrocortisone, whereas class 1 steroids are very potent – up to 600 times as potent as hydrocortisone (Oakley, 2009). Very potent steroids (i.e., class 1) are the most effective type of topical treatment, with a meta-analysis showing they have a response rate of 78% (i.e., of people) achieving at least 75% reduction in PASI score over the short-term (2 – 4 weeks) when applied twice daily (Samarasekera, Sawyer, Wonderling, Tucker, & Smith, 2013). In comparison, class 2 steroids have a response rate of 62% over this period. However, improvements from topical steroid use are usually not long-lasting after withdrawal of treatment (Samarasekera et al., 2013). Topical steroids are generally safe, but also have side effects and risks, including risk of rebound (worsening of disease after treatment discontinuation), development of stretch marks, skin thinning, and tachyphylaxis (decreased response to the drug) after long-term use (Mason et al., 2013).

Vitamin D analogues

The vitamin D analogue calcipotriol, branded as ‘Daivonex’ in New Zealand, is also a commonly prescribed treatment for mild-to-moderate psoriasis (Menter et al., 2008b).

Calcipotriol can reduce scaling and overall appearance of plaques, and was developed as an alternative to topical calcitriol to avoid its potential calcaemic effects (Shahriari, Kerr, Slade, & Grant-Kels, 2010). The response rate for at least 75% improvement of PASI has been reported as 54% when used twice daily over four weeks (Samarasekera et al., 2013), but it is often used in conjunction with a class 2 topical steroid, as this is more effective than either treatment alone (response rate of 71%) (Mason et al., 2013; Samarasekera et al., 2013). To this end, a combined corticosteroid/calcipotriol treatment has also been developed, and is called 'Daivobet' in New Zealand. There is good support for the safety of vitamin D analogues for up to 12 months' continuous use (Kragballe et al., 2006) but they are known to cause skin irritation in many people, and tachyphylaxis is common (Cohen et al., 2012).

Other topical treatments

Coal tar has been used to treat psoriasis for the past hundred years (Menter et al., 2008b). The types of preparations that are available have come a long way since the days when crude coal tar was used, causing great mess and significant irritation. Twice daily use of coal tar has a moderate rate of response for a 75% improvement in PASI (55%), but when used once daily it is usually no better than placebo (Samarasekera et al., 2013). Of all treatments, it has perhaps the least pleasant sensorial aspects, as it has a pungent smell that many are averse to, can stain skin and clothing, and can irritate skin at high concentrations and in some people (Menter et al., 2008b). Some people also develop dermatitis or inflammation of the hair follicles on contact (Menter et al., 2008b).

Salicylic acid is often found in therapeutic shampoos, and its main outcome is reduction of scaling, which can be helpful in allowing other treatments to penetrate the area, particularly in those with very thick plaques (Cohen et al., 2012). Used alone, it effectively clears psoriasis in only 3% of people, but in combination with topical steroids it can lead to clearance for up to 84% of people, which is slightly more than for topical steroids alone (Shokeen, O'Neill, Taheri, & Feldman, 2014). While salicylic acid appears to be one of the safer treatment options, application to more than 20% of the body surface or use in people with abnormal liver or kidney

function can lead to toxicity, due to absorption through the skin (Menter et al., 2008b).

Other less common topical treatments include retinoids and dithranol, both of which can cause significant skin irritation (Menter et al., 2008b). Dithranol, in particular, is useful for large, thick plaques through which other treatments would not penetrate (Cohen et al., 2012), and has a response rate of 43% for a 75% improvement of PASI (Samarasekera et al., 2013). On the other hand, retinoids have been found to be comparable to a placebo in efficacy (Samarasekera et al., 2013), and cannot be used during pregnancy as they are a known teratogen (Cohen et al., 2012).

2.8.2. Phototherapy

Treatment with sunlight, or ‘heliotherapy’, has been used over many centuries in the treatment of skin diseases (Hönigsmann, 2013). The modern-day use of phototherapy to treat psoriasis began in 1923, when William Henry Goeckerman published his regime of exposing skin to artificial broadband UVB (BUVB) light (290 – 320 nm) from a high-pressure mercury lamp alongside the use of coal tar (Hönigsmann, 2013). It was later determined that BUVB alone could clear mild forms of psoriasis when given in doses that produced slight erythema (Hönigsmann, 2013). The mechanisms by which UVB exposure improves psoriasis are still not completely understood, but are thought to primarily relate to its immunosuppressing effects (Halliday, Norval, Byrne, Huang, & Wolf, 2008). However, it also raises serum levels of vitamin D (Osmancevic et al., 2010), and vitamin D can also modulate the immune response (Baeke et al., 2010).

In the 1970s, a treatment regime combining oral psoralen or psoralen baths with high intensity ultraviolet-A exposure was found to be very effective at treating psoriasis, and became known as PUVA (Hönigsmann, 2013). This led to further research into phototherapy options for dermatology and the subsequent discovery of narrowband UVB (NUVB; 311 – 313 nm) (Hönigsmann, 2013). Narrowband UVB leads to complete clearance of psoriasis in a higher proportion of people than BUVB (68% [95% CI 57 – 78%] vs. 59% [95% CI 44 – 72%]; mean

percentage achieving clearance from studies assessing treatment over 4 – 24 weeks) (Almutawa, Alnomair, Wang, Hamzavi, & Lim, 2013), and is much easier to implement than PUVA (Hönigsmann, 2013). PUVA treatment has since fallen into decline, partly due to the introduction of NUVB (Hönigsmann, 2013), and also possibly due to the increase in risk of skin cancer after excessive exposure (> 350 treatments) compared to receiving < 150 treatments (Stern, 2012). Today, NUVB is the most preferred type of phototherapy for psoriasis, mostly used for patients in whom psoriasis is widespread across the body and cannot be controlled by topical treatments, but also for those with more limited, yet physically debilitating symptoms (Menter et al., 2010).

Long-term use of UVB phototherapy is usually necessary for maintenance as it does not promote permanent clearance (Naldi & Rzany, 2009) but it leads to premature ageing of the skin, and has the potential to increase cancer risk (Menter et al., 2010). Another notable disadvantage is the time required to undergo treatment and the consequent disruption to daily/work life, particularly as phototherapy facilities are often located at a distance from patients' homes (Menter et al., 2008a).

2.8.3. Conventional systemic treatments

Another treatment option for those with moderate-to-severe disease is one of the oral systemic therapies, namely methotrexate or ciclosporin, which are general immunosuppressants, or acitretin, a retinoid. No trials are available assessing the efficacy of these treatments over the long-term compared to a placebo (Nast, Jacobs, Rosumeck, & Werner, 2015). In separate retrospective studies in which the respective efficacies of particular systemic treatments were compared with other treatments, 27% of people on acitretin ($n = 62$), 46% of people on ciclosporin ($n = 36$) and 40 – 49% on methotrexate achieved a 75% improvement in PASI score after 12 weeks (Gisondi, Cotena, Tessari, & Girolomoni, 2008; Inzinger et al., 2013; Piaserico et al., 2014). Among those on methotrexate, 62% had achieved a 75% improvement in PASI at 24 weeks, and 81% had achieved this at one year (Inzinger et al., 2013).

Systemic treatments are each associated with safety concerns, especially if used over the long-term (Menter et al., 2009). Methotrexate can lead to hepatotoxicity (liver damage) and pneumonitis (inflammation of the lungs) (Menter et al., 2008b). It is associated with drug interactions leading to bone marrow suppression, and is also a teratogen, can induce spontaneous abortion, and reduces sperm count in males (Menter et al., 2008b). Use of ciclosporin over the long-term can cause impaired kidney function, hypertension and possibly increase development of non-melanoma skin cancer and lymphoma (Menter et al., 2008b). Acitretin is teratogenic, has adverse effects such as dry fragile lips, skin, nose and eyes, peeling palms and soles, hair loss, thinned fragile nails, and delayed wound healing, and it also may cause dyslipidemia and joint pain (Lee & Li, 2009).

2.8.4. Biological therapies

Biological therapies, which are used for the treatment of more extensive psoriasis, have only become available in recent years. They are called biological therapies, or biologics, as they are engineered from living materials such as human and mouse antibodies (Stinco & Errichetti, 2015). They differ from traditional systemic therapies in that rather than suppressing the overall immune system, they directly target and suppress specific immune responses involved in psoriasis (Lebwohl, 2005). The range of biologics currently available includes adalimumab (Humira), etanercept (Enbrel) and infliximab (Remicade), which suppress TNF- α ; ustekinumab (Stelara), which is an antibody against IL-12 and IL-23 (Papoutsaki & Costanzo, 2013); and secukinumab (Cosentyx), which inhibits IL-17 (Blauvelt, 2016). They are delivered by injection or intravenous infusion, usually on a weekly or fortnightly basis.

Biologics have the highest efficacy rate of psoriasis treatments that have been developed so far, with the relative response rates for clear or almost clear skin when compared to methotrexate and UVB phototherapy ranging from 1.45 [95% CI 1.06 – 1.97] for etanercept to 2.15 [95% CI 1.60 – 2.90] for adalimumab (Gelfand et al., 2012). Compared to a placebo, the probability of achieving at least 75% improvement in PASI ranges from 8.4 (95% CI 6.7 – 10.5) for etanercept

to 13.1 (95% CI 8.6 – 19.9) (Nast et al., 2015). However, as for other treatments, the proportion of people achieving this degree of clearance is widely variable: between 44% and 89% on adalimumab, 49% and 92% on etanercept and 66% on ustekinumab achieved at least 75% clearance with long-term treatment (1 – 2 years) (Zweegers et al., 2016). Seventy percent of people on infliximab for between 16 and 28 weeks also achieved at least 75% improvement in psoriasis (Zweegers et al., 2016). Short-term efficacy (over 12 – 16 weeks) is lower than efficacy over the longer-term for all biologic treatments (Zweegers et al., 2016). Full clearance from biologics has been found to be achieved in between 34% and 48% of people (Gelfand et al., 2012), and it has been suggested that the relatively greater efficacy of biologics compared to methotrexate (with which 24% of people achieved full clearance) might not translate into a clinically meaningful difference between biologic and systemic treatments (Gelfand et al., 2012).

All biologics promote an increased risk of infection, particularly upper respiratory tract infections, and possibly the risk of developing demyelinating disorders such as multiple sclerosis, liver disease and some cancers; they may also have the potential to induce lupus-like syndromes (Menter et al., 2008a). Although serious infections leading to hospital admission or death are not common, patients who have underlying co-morbidities (which are more common in psoriasis) are at higher risk (Papoutsaki & Costanzo, 2013). As biologics are very expensive, their use is limited to those with moderate-to-severe psoriasis in whom all other treatments have failed, the side effects of other treatments have become intolerable or toxicity has occurred, or who have other medical conditions which prevent the use of traditional systemic therapies (My Psoriasis, 2015).

2.9. Summary and conclusions

Psoriasis is a complex, unpredictable condition that is not consciously preventable in those who are genetically predisposed. Attempts to elucidate the aetiology of psoriasis have proved this to be a slow-moving and challenging process, but breakthroughs over time have led to the use and

development of important treatments. Despite this, all available treatments have drawbacks, from the inconvenience and short duration of remission in topical treatments, to the risks associated with prolonged exposure to UVB light, to the immunosuppressing actions of conventional systemic and biologic treatments, not to mention the cost of the more advanced therapies. So long as there continues to be no treatment that combines efficacy in treating psoriasis with minimal (or no) inconveniences, risks, side effects or high costs, there will be no alternative for many people with psoriasis but to continue to struggle with managing their skin over the long-term. The well-established level of evidence around the burden of psoriasis, as briefly introduced in Chapter 1 of this thesis, suggests that this will mean the ongoing likelihood of significant adverse impact on people's lives through the many-faceted implications that accompany living with psoriasis. This thesis now turns to understanding these implications in greater detail, with the two forthcoming chapters addressing the experience of living with psoriasis.

3. Study One: The Experience of Living with Psoriasis

This chapter provides the background and the theoretical and methodological approaches in relation to the first aim of this thesis, which is to gain a deeper understanding of the experience of living with psoriasis. In order to emphasise the importance of conducting further research in this area, the chapter opens with a discussion of previous research related to the experience of psoriasis. This ranges from quantitative research identifying the various aspects of life that can be influenced through having psoriasis, to qualitative research that has involved a more in-depth consideration of the experience overall. This leads into a discussion of the epistemological and methodological considerations of conducting research into the experience of psoriasis, including an overview of the approaches that have previously been taken towards research in this area.

3.1. Living with psoriasis

The experience of living with psoriasis has been a gradually increasing focus of research since the 1970s. Early interview-based research provided examples of the many ways in which psoriasis created difficulties in everyday life through not only its physical, but also its psychosocial and emotional effects (Jowett & Ryan, 1985). Consequently, the previously held view of psoriasis as merely a bothersome skin condition began to give way to greater acknowledgement of the wider implications of psoriasis for a person's wellbeing, and also to the appreciation that clinical psoriasis severity does not necessarily determine its impact (Lebwohl, 2005). It is now accepted that psoriasis can have profound consequences for a person's physical, psychological, social and even vocational wellbeing, and can therefore influence almost every aspect of a person's life.

The purpose of this section is to discuss what previous research has shown about the experience of living with psoriasis, in order to demonstrate the importance of undertaking further research in this area. It begins by discussing the impact of psoriasis in relation to people's overall quality of life, to illustrate the relative magnitude and extent of the perceived burden of psoriasis. This is followed by a critical discussion of the implications of psoriasis on the physical, psychosocial

and emotional realms of life, and then of people's experiences using treatments and engaging with healthcare providers. Finally, this section discusses what is known about the experience of psoriasis over time, and the factors that influence people's ability to adjust to life with the disease. The focus of this section will predominantly be on the *findings* of previous studies; greater consideration of the different methodological approaches that have been taken in regards to understanding the psoriasis experience will be given in the Methodology section (3.2) that follows.

3.1.1. The impact of psoriasis on quality of life

The burden of psoriasis is often described in terms of the degree that it impacts the quality of life of people with the disease. Commonly, this is assessed by way of questionnaires that measure a person's perceived impact of psoriasis symptoms and treatments in relation to a range of life dimensions, including physical, emotional and social wellbeing, and the ability to perform daily, leisure, work and/or school activities (Bronsard et al., 2010). Findings from research using these questionnaires and similar have unequivocally confirmed the significant negative impact that psoriasis can have across these various realms of life (Anstey et al., 2012; Krueger et al., 2001). On average, people with psoriasis report a lower quality of life overall than those in the general population (Badia, Mascaró, & Lozano, 1999; Baker et al., 2013; de Korte et al., 2004; Lundberg, Johannesson, Silverdahl, Hermansson, & Lindberg, 1999; Rapp et al., 1999; Reimus, Vingerhoets, Soons, & Korstanje, 2007; Weiss et al., 2002). This is particularly the case for those with active compared with stable psoriasis (Dauden et al., 2013), and quality of life is even further reduced in those who also have psoriatic arthritis (Lundberg, Johannesson, Silverdahl, Hermansson, & Lindberg, 2000). Furthermore, reported life quality across people with psoriasis has been shown to be reduced to similar levels as in those with other serious, even life-threatening illnesses such as cancer, chronic lung disease, diabetes, post-myocardial infarction, depression (Rapp et al., 1999), and chronic congestive heart failure (Baker et al., 2013), and is lower in those with psoriasis compared to people with sub-syndromal bipolar depression or stable human immunodeficiency virus (Baker et al., 2013). In

those who also have two or more co-morbidities, it is reduced even further, to a similar degree as people with stable, but advanced gastric cancer (Baker et al., 2013). From another perspective, people with psoriasis have indicated that they would be willing to accept significant risk of serious infection, tuberculosis and lymphoma if it meant they would achieve complete clearance of even clinically mild psoriasis affecting a quarter of their skin, with the level of acceptable risk greatly increasing alongside the extent and severity of psoriasis (Kauf et al., 2015).

As psoriasis is not typically thought of as a serious condition, the degree to which it can impact quality of life is perhaps surprising. Even more surprising may be that the considerable burden of psoriasis is not limited to people with more severe forms of disease, but can even affect those whose psoriasis is at minimal levels. This is clearly illustrated by findings of a survey of the US population ($n = 27,220$, of whom 601 had psoriasis), in which 60% of those for whom psoriasis was a substantial problem in their daily lives had less than three palm-sized areas of affected skin (Stern et al., 2004). Even participants who had only one or two palm-sized areas of psoriasis had significantly lower quality of life than those with none or very minimal psoriasis (Gelfand et al., 2004). Furthermore, when extrapolated to population-wide figures, nearly half a million people were estimated to consider their psoriasis as a large problem in everyday life, even though the prevalence of those with clinically severe psoriasis in the US at the time was only approximately 120,000 people (Stern et al., 2004). Conversely, some people with more clinically severe psoriasis report no burden of psoriasis on their lives (Norlin, Steen Carlsson, Persson, & Schmitt - Egenolf, 2012). Consequently, while some findings have shown a relationship between the severity of psoriasis and quality of life (Norlin et al., 2012), in many studies these have been unrelated (Fortune, Main, O'Sullivan, & Griffiths, 1997; Heydendael et al., 2004; Richards, Fortune, Griffiths, & Main, 2001; Weiss et al., 2002), indicating that any relationship that may exist between these factors is not straightforward. Findings such as these demonstrate that it is not only clinical severity that influences how significantly people are impacted by psoriasis; instead, a complex mix of factors influences the way a person

experiences living with the disease (Fortune, Richards, Main, & Griffiths, 2002), and the remainder of this review is based around discussing these different factors.

Although the clinical severity of psoriasis is not always related to the degree of perceived impact of psoriasis, quality of life can improve following effective treatment (Lee, Park, Kwon, Kim, & Kim, 2010; Shear et al., 2016). Improvements in quality of life relate not only to a reduction in psoriasis symptoms, but also to fewer daily hassles and less psoriasis-related stress (Fortune et al., 2004; Takahashi, Iinuma, Tsuji, Honma, & Iizuka, 2014). Biologic treatments seem to bring about greater improvements in quality of life compared to systemic or topical treatments, irrespective of the degree of improvement in clinical severity (Takahashi et al., 2014). This may relate to their greater efficacy in relation to treating scalp and nail psoriasis – as the extent of scalp and nail psoriasis is difficult to capture with PASI but these have an appreciable impact on quality of life (Takahashi et al., 2014) – as well as their ease of use in comparison to topical treatments. The magnitude of improvement in life quality also appears to be greatest in those for whom psoriasis is severe; for example, in one study, people with more severe psoriasis had an improvement in life quality that was twice as great as for those with milder psoriasis (Fortune et al., 2004). There is a clinically meaningful difference in reported quality of life between those who achieve complete clearance and those who still have very minimal psoriasis, with the latter still experiencing some degree of burden as a result of their symptoms (Strober et al., 2016), showing that the extent to which the physical symptoms of psoriasis improve has a bearing on the degree of change in quality of life. Such findings emphasise the benefit that can be gained through achieving clearance of psoriasis.

Findings related to quality of life in people with psoriasis demonstrate that in general, people with psoriasis experience a significant negative impact of the disease across their lives overall, and that numerous personal, disease-related and environmental factors influence the degree to which people see psoriasis as affecting their quality of life. While research of this kind can indicate the average degree to which people consider psoriasis to be a burden, as well as some of the factors that influence this, this type of research does not offer any insight into the detailed

experience of living with psoriasis. This review will now turn to a more in-depth discussion of different aspects of the psoriasis experience, in which findings from qualitative studies that have provided a richer understanding of experience will be considered alongside quantitative findings.

3.1.2. The physical burden of psoriasis

The impact of psoriasis on physical functioning can be an important contributing factor to reduced quality of life those with the condition (de Korte et al., 2004; Ljosaa, Mork, Stubhaug, Moum, & Wahl, 2012; Norlin et al., 2012; Rapp et al., 1999). Issues related to physical functioning in psoriasis include symptoms and their impact on daily activities, mobility, energy/vitality and sleep and rest (de Korte et al., 2004). Itch, flaking skin and/or pain are reported to be some of the most common and difficult symptoms to deal with by people with both mild and severe psoriasis (de Korte et al., 2004; Globe et al., 2009). Itch is, at best, a bothersome symptom, but some people consider its intensity and incessancy to be unbearable (Amatya, Wennersten, & Nordlind, 2008), and having severe itch makes people more likely to view their psoriasis as having a major negative impact on their lives regardless of its clinical severity (Fortune, Richards, Main, & Griffiths, 1998; Ljosaa et al., 2012). This is likely to be due to itch having far-reaching implications, interfering with sleep, appetite and libido, as well as a person's ability to concentrate and attend work or school (Amatya et al., 2008; Globe et al., 2009). It is also accompanied by the desire to scratch, which can lead to feelings of being negatively judged by others (Reich, Hrehorow, & Szepietowski, 2010). Pain and/or discomfort due to psoriasis can also occur regardless of the severity of psoriasis, and also contribute to reduced enjoyment of life (Ljosaa et al., 2012). Pain arising from plaques has been variously described as dull, sharp, throbbing, stinging and/or stabbing by people with clinically moderate-to-severe psoriasis (Martin et al., 2015). More elaborate descriptions have included "painful like an open sore", a "dreary, steady pain", "like a friction burn" and "tender, like a bad sunburn" (Martin et al., 2015, p. 403). Affected skin has been described as feeling irritated and itchy, and scratching could lead to pain that is "burning" or "aching" (Martin et al., 2015, p.

403). Skin pain can lead to feelings of despondence, irritation and despair, and itching, swelling, burning sensations and flaking skin also contribute to low mood (Wahl, Gjengedal, & Hanestad, 2002).

The physical symptoms of psoriasis can also bring about considerable practical inconveniences and disruptions to people's daily lives (Krueger et al., 2001). Many people with psoriasis, and the majority of those who also have psoriatic arthritis, have reported physical difficulties such as using hands or walking, or sitting or standing for long periods, and this may be particularly the case in older people (Krueger et al., 2001; Tadros et al., 2011). People with psoriasis have described never feeling "fresh", and instead, feeling messy and unclean because of the presence of plaques and the sensation of topical treatments on their skin (Uttjek, Nygren, Stenberg, & Dufåker, 2007, p. 369). The use of messy ointments and lotions, as well as bloodstains from cracked skin, means that clothes often need to be changed much more frequently than normal, and the prolific flaking of skin can necessitate more household cleaning (Khoury, Danielsen, & Skiveren, 2014; Wahl et al., 2002). Problematically, the physical aspects of psoriasis can make it difficult to perform household chores, particularly physically demanding activities such as vacuuming, and tasks involving skin-contact with water, and many people report needing assistance with these tasks (Leino, Mustonen, Mattila, Koulu, & Tuominen, 2015). Pain and itch/scratching contribute to sleep-related difficulties such as broken sleep and decreased sleep quality (Gowda, Goldblum, McCall, & Feldman, 2010). Relatedly, feelings of fatigue are commonly experienced, and both fatigue and sleep-related difficulties have a negative impact on people's overall quality of life (Evers et al., 2005; Ljosaa et al., 2012).

Understandably, the physical burden is usually even greater in those who experience psoriatic arthritis alongside their psoriasis (Krueger et al., 2001; Uttjek et al., 2007; Warren et al., 2011). Joints affected by psoriatic arthritis tend to be warm and swollen, to cause significant pain and discomfort and, as mentioned above, to cause significant limitations to mobility in the majority of sufferers (Krueger et al., 2001; Mease & Menter, 2006). The experience of joint pain from psoriatic arthritis has been described as feeling "like your fingers are broken", which can be felt

“inside your bones” (Martin et al., 2015, p. 402), and for some people, this pain is present all day and night (Uttjek et al., 2007; Warren et al., 2011). In case studies of people with moderate-to-severe psoriasis, Warren et al. (2011) identified the greater life significance of consequences that can arise from the physical limitations of psoriasis. One participant experienced severe flare-ups that prevented him from playing with his children at the park, and interfered with other aspects of family life (Warren et al., 2011). For another, physical limitations from psoriatic arthritis became so severe that she could move no further than from her bed to a chair, which led to obesity and therefore other significant negative repercussions for her life (Warren et al., 2011).

From the evidence presented here, it can therefore be concluded that the physical symptoms of psoriasis, while perhaps seemingly minor on the surface, can have major implications for a person’s ability to go about their daily activities, to get adequate rest, and to get enjoyment from life. One participant in an interview-based qualitative study (Watson & de Bruin, 2007) illustrated how all-consuming these physical symptoms could be by summing up her experience as follows:

Before long, my legs and arms were covered, some on my bum, lower back and most uncomfortable, my ears. Psoriasis is very, very sore. The itchiness drives you mad. You can’t sleep and you scratch your arms and legs to pieces...I started cortisone injections into the lesions every 6 weeks. You have no idea how painful that is. You bleed continuously and the lesions look so ugly for 2 to 3 days and you are in a lot of pain. (p. 355)

3.1.3. The psychosocial burden of psoriasis

In addition to causing physical difficulties, psoriasis is also frequently detrimental to the psychosocial and emotional wellbeing of sufferers (Feldman, Malakouti, & Koo, 2014; Sampogna et al., 2006). For many people, living with psoriasis can have a considerable negative psychological impact (Fouere et al., 2005; Sampogna et al., 2006), and it can bring

about feelings of distress on a frequent or even daily basis (Nash et al., 2015). Such distress can take many and variable forms, with feelings of embarrassment, shame, humiliation, annoyance, depression, anger, frustration, sadness, hopelessness, desperation and despair all having been expressed in relation to psoriasis (Bundy et al., 2014; Sampogna, Tabolli, & Abeni, 2012). Worry that psoriasis might worsen or cause scarring is also common (Sampogna et al., 2012), as is guilt at the thought of passing it on to one's children (Young, 2005). Women appear to suffer psychologically in relation to their psoriasis to a greater extent than men (Daudén et al., 2013; Finzi et al., 2007; Fortune et al., 1998; Gelfand et al., 2004; Norlin et al., 2012; Obradors, Blanch, Comellas, Figueras, & Lizan, 2016; Ograczyk, Miniszewska, Kępska, & Zalewska-Janowska, 2014), possibly due to the greater emphasis on physical appearance in women (Öberg & Tornstam, 1999), which could mean psoriasis has a more negative impact on their self-esteem (Picardi et al., 2001).

Many people with psoriasis also experience significant levels of psychological stress (Finzi et al., 2007), and clinically relevant depression and anxiety in relation to living with the condition (Gupta & Gupta, 1998; Hayes & Koo, 2010). Those with psoriasis who report a greater degree of stress or impaired quality of life tend to have more visibly disfiguring psoriasis (Dauden et al., 2013), or psoriasis that affects more 'emotionally charged' areas such as the face, hands and genitals (Gupta & Gupta, 2003; Ryan et al., 2015). Stress can present a particular challenge in people with psoriasis, as for many, stress also exacerbates the disease, creating a vicious cycle that is difficult to get out of (Basavaraj, Navya, & Rashmi, 2011; Kouris et al., 2015). Anxiety linked to psoriasis is particularly related to the potential social implications of psoriasis, such as a fear of being judged by others (Hayes & Koo, 2010); these implications will be elaborated on further below. The severity of depression has been related to the intensity of itch (Reich et al., 2010), having more severe psoriasis (Gupta & Gupta, 1995, 2003), and the overall perception that psoriasis has a negative impact on one's life (Gupta & Gupta, 1995, 2003). Of great concern, relatively high rates of suicidal ideation have also been found in people with psoriasis, particularly those with more severe psoriasis, compared to the prevalence among general

medical patients (Gupta & Gupta, 1995; Krueger et al., 2001).

Central to the psychological impact of psoriasis is how a person feels about the appearance of their psoriasis, which typically engenders feelings of embarrassment and shame, and low levels of confidence and self-esteem (Magin, Adams, Heading, & Pond, 2009b; Sampogna et al., 2012; Weiss et al., 2002). To try and minimise such feelings, most people try and keep their psoriasis hidden from others by avoiding certain activities and limiting themselves to particular styles of clothing (Nash et al., 2015; Young, 2005); for example, wearing long sleeves and pants to cover their arms and legs, and avoiding dark-coloured clothing so falling scales are less visible. Activities that are avoided often include things that a person would otherwise choose to do, such as attending social events, participating in sports and visiting the hairdresser (Globe et al., 2009; Nash et al., 2015). It is not only from acquaintances and the general public that people try to keep their skin hidden; the findings of a recent Australian survey showed that a significant percentage of people also hide their psoriasis from family members, close friends and their spouse or partner (Baker et al., 2013). Some people even report that they feel too embarrassed to go out in public (Nash et al., 2015). While keeping psoriasis hidden from others may help people to avoid difficult feelings in the short-term, such behaviours have been related to lower quality of life (Rapp, Cottrell, & Leary, 2001), probably because they promote stress (Fortune et al., 1997) and do not allow the opportunity for negative beliefs about themselves to be disconfirmed (Thompson & Kent, 2001), thus perpetuating issues with self-confidence. Participants in qualitative interviews have offered insight into other consequences of these types of behaviours for their lives, ranging from extreme discomfort and even handicap arising from having to wear winter clothing in summer, to sadness about missing out on simple pleasures such as walking on the beach in shorts and a t-shirt (Khoury et al., 2014). For some, avoiding physical activity to keep their psoriasis hidden meant giving up a sport they loved and had played for most of their life; for others, it meant obvious detriment to their health through development of obesity and high blood pressure (Khoury et al., 2014).

As having psoriasis can impact so greatly on people's self-confidence, many find it difficult to make new friendships and sustain existing ones (Anstey et al., 2012). The findings of several studies suggest that younger people are negatively impacted by psoriasis to a greater degree than older people (Fernandez-Torres, Paradela, & Fonseca, 2012; Gelfand et al., 2004; Norlin et al., 2012), and specifically in relation to social wellbeing (Krueger et al., 2001), which probably relates to the psychosocial implications of having a visible skin disease during critical periods of social development. In line with the social difficulties that can arise in relation to psoriasis, people with psoriasis often describe feelings of loneliness and social isolation (Kouris et al., 2015; Nash et al., 2015). Related to such feelings are people's perceptions that they are not understood by others, and that others cannot comprehend what it is like to live with psoriasis (Linder et al., 2009; Young, 2005). Some people even attribute psoriasis with causing them to become permanently shy, withdrawn and introverted (Magin et al., 2009a).

Perhaps unsurprisingly then, psoriasis and its related self-consciousness, impaired self-confidence and effect on self-esteem can also contribute to difficulties pursuing and sustaining intimate relationships, with psoriasis inhibiting sexual activity and wellbeing (Anstey et al., 2012). Skin that is shedding and flaking, and the unbecoming use of treatments, commonly contribute to feelings of unattractiveness and a reduced desire for intimacy; again, particularly in those who are of younger age (Baker et al., 2013; Gupta & Gupta, 1997; Khoury et al., 2014; Krueger et al., 2001). Painful, stinging and cracked psoriatic lesions can also promote a reluctance to engage in sexual activities because of fears of infection (Khoury et al., 2014). Even those in long-term partnerships can be affected, with low self-esteem leading to sexual inhibition and avoidance of intimacy (Khoury et al., 2014; Magin, Heading, Adams, & Pond, 2010). Yet, those who are single tend to experience even greater problems around intimacy (Young, 2005), expressing discomfort at the idea of skin being "on show", and reluctance towards starting a new sexual relationship, in part, for fear of rejection (Magin et al., 2010, p. 457). Some have even stated that beginning a new relationship is out of the question so long as their psoriasis remains visible (Khoury et al., 2014; Magin et al., 2010).

Stigmatisation

One of the foremost contributors to the psychological morbidity arising from psoriasis is a fear of being stigmatised on the basis of appearance (Magin et al., 2009a). Embarrassment, shame, and other emotions that people experience in relation to the appearance of psoriasis have been directly linked to concerns about being scrutinised and judged on one's internal worth, being thought of as less hygienic, and being worried that others might think they are contagious (Magin et al., 2009a). These concerns are not unfounded, as the majority of people with psoriasis experience significant feelings of being stigmatised and/or overt incidences of stigmatisation because of their appearance at some point in their lives (Baker et al., 2013; Hrehorow et al., 2012). Examples of stigmatisation experienced by people with psoriasis include having difficulties receiving equal service or treatment at public facilities such as hair salons and barbers, swimming pools and gyms (Nash et al., 2015), for instance because of people fearing they are infectious, and even being excluded from public facilities for this reason (Krueger et al., 2001). These types of experiences are central to the development of avoidance behaviours around psoriasis, as people learn to anticipate rejection and try to minimise it by avoiding situations in which it might occur (All Party Parliamentary Group on Skin, 2003).

In one sense, stigmatisation towards psoriasis can be related to the widespread lack of understanding that surrounds the disease. This is illustrated by findings of a recent US study, in which people were shown unidentified pictures of psoriasis with the aim of assessing attitudes and opinions of the lay public towards its appearance (Donigan et al., 2015). Nearly 61% of participants assumed that it had an infectious cause; furthermore, over half said they would avoid touching someone with the condition (Donigan et al., 2015). Yet, stigma towards psoriasis appears to arise not only from unwarranted fears of contagion, but also from the incompatibility of the appearance of psoriasis with societal standards around attractiveness and beauty. Half of participants in the same study said they would find someone with psoriasis unattractive, and more than a third would feel uncomfortable being seen with that person in public (Donigan et al., 2015). Females with psoriasis, especially, see the idea that skin should

be flawless as significantly contributing to their experiences of stigmatisation, and they have described feelings of resentment towards the media for the perpetuation of such ideals (Magin, Adams, Heading, & Pond, 2011). Furthermore, even when this ideal is viewed as unrealistic, and even false and manufactured, people with psoriasis have described being unable to avoid personally 'buying in' to such ideals (Magin et al., 2011). Consequently, many people become preoccupied with their appearance, and hypervigilant in their efforts to try and maintain an appearance that is as close to 'ideal' as possible (Thompson & Kent, 2001). In spite of such efforts, the discrepancy between psoriasis and societal ideals around appearance and the feelings of stigmatisation that arise from this can contribute to low self-esteem, depressed mood, and a negative image of one's body (Khoury et al., 2014; Magin et al., 2011; Magin et al., 2010).

For some people, a negative body image translates into a fundamentally negative self-image (Khoury et al., 2014; Wahl et al., 2002). That is, through viewing their bodies as, for example, "offensive, unclean, infectious, disgusting, leprous, ugly, unattractive, strange, gross or different" because of their psoriasis, people can also view themselves as that way overall (Wahl et al., 2002, p. 254). Relatedly, some people have described how psoriasis has 'shaped' them, in that the lines between themselves and psoriasis have become blurred and they have started to view their psoriasis as themselves (Bundy et al., 2014). For others, the impact of psoriasis on self-image varies with the degree that it is visible; they can effectively function as 'normal' in times when symptoms are minimal, yet not when symptoms are severe (Wahl et al., 2002). As suggested by the degree to which stigmatisation towards psoriasis can impact people's self-esteem, the self-image of people with psoriasis can be highly susceptible to the influence of others, with how they feel about themselves dependent on the reactions from those with whom they interact (Khoury et al., 2014; Wahl et al., 2002). At the same time, some people attribute opinions that they have about themselves to others and therefore think that other people view their bodies negatively, which 'confirms' these negative thoughts and worsens their self-image (Khoury et al., 2014; Wahl et al., 2002).

As self-esteem and self-image in people with psoriasis can be easily influenced by how others react towards their skin, it follows that they can also be significantly affected by intentional acts of stigmatisation towards psoriasis such as teasing, taunting and bullying (Magin, Adams, Heading, Pond, & Smith, 2008). Hurtful experiences of this nature have included being ridiculed because of appearance or for having 'leprosy' or 'syphilis', and being excluded from social groups (Magin et al., 2008; Uttjek et al., 2007). While experiences of teasing or bullying can occur at any age, they are more common during childhood and adolescence, and experiencing this type of stigma when young can have a long-lasting detrimental impact on psychological wellbeing (Magin et al., 2008; Uttjek et al., 2007).

In summary, for many people, the psychosocial and emotional burden is the most challenging aspect of living with psoriasis. In particular, embarrassment, shame and feelings of stigmatisation arise for most people in relation to the appearance of psoriasis, and some also report overt experiences of being stigmatised by others. As a consequence, most people tend to try and hide their psoriasis, and avoid activities in which others might see their skin, which often means living a less fulfilled life. The way a person feels about the appearance of their psoriasis often leads to low levels of self-confidence and self-esteem, and can consequently interfere with the development and maintenance of social and intimate relationships. Further, people often view their bodies in a negative light because of the appearance of psoriasis, which can lead them to have a negative view of themselves overall.

3.1.4. The impact of psoriasis on work, career and education

The impact of psoriasis is frequently considered to flow into people's work lives, attributed with reducing their productivity, income and earning potential (Ayala et al., 2013; StollzNow Research, 2013). Numerous work days can be lost due to the need to attend appointments and/or receive phototherapy treatments (Ayala et al., 2013), and a loss of productivity due to psoriasis while on the job has been also described (Pearce et al., 2006), which worsens with

increased levels of itch, pain and flaking skin (Lewis-Beck, Abouzaid, Xie, Baser, & Kim, 2013).

Many people also see their psoriasis as restricting their employment opportunities, chance for promotion and range of career options (Anstey et al., 2012; Krueger et al., 2001; Nash et al., 2015). In a survey of New Zealand Psoriasis Association members, 25% of women and 10% of men stated that their psoriasis had prevented them from accepting a job, often because of not being able to cover their psoriasis in the role, or being worried about catching a disease through their skin flaking (StollzNow Research, 2013). The perception that certain career options are closed off also arises from a desire to avoid negative reactions from others (Jowett & Ryan, 1985). For example, a sportswoman felt unable to become a physical education teacher because of concerns about how others would react to her psoriasis; similarly, a trainee psychiatric nurse felt psoriasis prevented an entry into general nursing, and others felt that a career in catering was off limits to them (Jowett & Ryan, 1985). Some people have felt their psoriasis was a factor in a job interview being unsuccessful (Jowett & Ryan, 1985), experiencing discrimination at work (Warren et al., 2011), or losing their job (Anstey et al., 2012; Krueger et al., 2001), and these types of experiences have prevented people with psoriasis from following or continuing their chosen career paths. On average, the more psoriasis lesions people have, and the more they feel shame, anger and experience low self-esteem as a result of having psoriasis, the more they see psoriasis as causing limitations around work (Ayala et al., 2013). Psoriasis has also been implicated in preventing people from undertaking or achieving their potential in higher education (Anstey et al., 2012; Warren et al., 2011), for some, as a direct consequence of becoming socially isolated because of their psoriasis (Warren et al., 2011).

3.1.5. The burden of psoriasis treatment and the struggle for control

For many people, the burden of psoriasis is compounded by the difficulty they have in trying to adequately manage it (Ersser et al., 2010). Psoriasis can be challenging to treat (Bewley & Page, 2011), and its disease course can be unpredictable, swinging between remission and

various degrees of severity (Menter et al., 2008a). Dissatisfaction with treatments abounds amongst people with both mild and more severe psoriasis, in part because of their perceived lack of ability to keep psoriasis under control and at minimal levels (Armstrong et al., 2013a; Baker et al., 2013; Fouere et al., 2005; Krueger et al., 2001; Stern et al., 2004). This is particularly the case for topical treatments, which are the most commonly used type of treatment for psoriasis and usually the only prescription treatment offered to those with mild disease (Menter et al., 2008a), but it also relates to systemic and biologic treatments (Yeung et al., 2013b). As psoriasis responds differently to treatments from person to person, finding one that works can be a long and consuming process of trial and error that can lead to frustration, disappointment, and a loss of faith in topical treatments by the time more potent varieties are prescribed (Bewley et al., 2014; Bundy et al., 2014). Treatment dissatisfaction may also be a consequence of people expecting those treatments to be more effective than they are; to illustrate, 32% of participants in one study believed that their prescribed treatments would be curative (Fortune et al., 1998).

The burden of psoriasis and the dissatisfaction with treatments are compounded even further still because of the many unpleasant side effects that have been associated with using psoriasis treatments (Nash et al., 2015). Difficulties that people experience using topical treatments have included the considerable length of time it can take to apply them (Leino et al., 2015), the fear of side effects (Fouere et al., 2005), and their inherent characteristics (oiliness/stickiness an off-putting smell and visibility) that then lead to feelings of being unclean (Bewley et al., 2014; Nash et al., 2015). Experiencing side effects, sometimes serious ones, have also been a commonly expressed reason for the cessation of systemic and biologic treatments (Yeung et al., 2013a), whereas the main factors causing dissatisfaction with phototherapy have been related to inconvenience and the financial and time cost (Yeung et al., 2013a). Consequent to these concerns, 'coping with treatments' has been identified as one of the most common problems that people experience in relation to psoriasis (Nash et al., 2015). In some people who developed psoriasis during childhood or adolescence, these negative aspects of treatments had

such a significant impact that they were later seen as having profoundly shaped those early years (Bundy et al., 2014).

The difficulties around managing psoriasis, including the off-putting side effects of treatments, its inability to be cured, and the uncertainty around its future course all contribute to the feelings of lack of control that people frequently feel in relation to psoriasis (Lamb, Fried, & Feldman, 2004; Nelson et al., 2013b; Wahl et al., 2002). The experience of psoriasis has been described as a constant struggle or battle to try and gain control over the disease (Bundy et al., 2014), while at the same time, psoriasis is seen as uncontrollable (Lamb et al., 2004; Linder et al., 2009; Magin et al., 2009a).

3.1.6. Experiences with healthcare providers

Further contributing to the burden of psoriasis is the perceived lack of support that people with psoriasis often experience from their health care practitioners (Ersser et al., 2010; Magin et al., 2009b; Nelson et al., 2013b). Across several studies, most prominent was the perceived lack of acknowledgement from health care practitioners of the stress and distress arising from the social and psychological aspects of psoriasis, particularly its associated social stigma and the feelings of powerlessness it generates (Bewley et al., 2014; Ersser et al., 2010; Magin et al., 2009b; Nelson et al., 2013b). This lack of acknowledgement can lead to anger towards healthcare professionals (Bundy et al., 2014), as well as perpetuate feelings of negativity towards one's appearance (Khoury et al., 2014), and a sense of low self-esteem (Bundy et al., 2014). People with psoriasis have expressed a strong need to feel supported by healthcare practitioners and for them to acknowledge the challenges of living with psoriasis, but these needs have often gone unfulfilled due to practitioners seeming to prevent the opportunity for emotional disclosure during consultations (Nelson et al., 2013b). Some people have felt dismissed by their doctors, and others have experienced unsympathetic or even derogatory attitudes, which has compounded the burden of psoriasis by leading to feelings of guilt and low self-esteem (Magin et al., 2008; Magin et al., 2009b). This perceived lack of support from healthcare practitioners

places additional strain on people and in some cases, has caused people to stop engaging with them (Nelson et al., 2013b).

Many people have also expressed feeling under-informed about their psoriasis, which then contributes to a sense of confusion and a general lack of direction in relation to their psoriasis (Bewley et al., 2014), and to the feeling of having no control over their condition (Nelson et al., 2013b). People have expressed wanting to be able to self-manage their psoriasis, but feel that they need to be empowered to do so by being educated by healthcare professionals about their condition, and to be supported along the way (Ersser et al., 2010). Yet many feel that general practitioners (GPs), but also some dermatologists, appear to lack expertise and interest in psoriasis (Ersser et al., 2010). Some people had the sense that their GP had given up on psoriasis because it could not be cured, and felt that attending follow-up visits was pointless because they were merely told to “go away and try this” (Ersser et al., 2010, p. 1046; Magin et al., 2009b). On the other hand, some related this to the inherent difficulties associated with treating skin diseases rather than it being the fault of the doctor (Magin et al., 2009b).

Thus, the evidence presented above suggests that, although treatments for psoriasis and support from healthcare professionals ideally mitigate some of the negative impact of psoriasis, and may have the potential to do so, it is often the case that they further contribute to the strain of living with the disease.

3.1.7. Adjustment to psoriasis

The majority of the literature that has been discussed so far in this review presents psoriasis as a burden, as indeed, most research into psoriasis has been focused on the many negative consequences of living with the condition. However, some people are able to adjust well to psoriasis, regardless of its clinical severity (Berth-Jones, 2013). Whether a person is able to adjust to living with psoriasis or not is influenced by a complex mix of disease-related, individual and environmental factors, but ultimately comes down to the nature of the way they personally view and respond to the disease (Fortune et al., 2002).

While it would be difficult, if not impossible, to determine every factor that affects a person's individual experience of psoriasis, some specific factors have been named as important in this regard. For instance, a person's perceptions of their psoriasis (Scharloo et al., 2000), their health-locus of control (i.e., whether or not they believe their health is determined by their own behaviour) (Miniszewska, Juczynski, Ograczyk, & Zalewska, 2013b), the coping strategies they use (Fortune et al., 2002; Ograczyk et al., 2014; Scharloo et al., 2000; Wahl, Hanestad, Wiklund, & Moum, 1999), and perhaps most importantly, their overall outlook on life (Miniszewska, Chodkiewicz, Ograczyk, & Zalewska-Janowska, 2013a), are fundamental to the way a person experiences psoriasis. Perhaps expectedly, those who have a more optimistic outlook (Miniszewska et al., 2013a), feel more self-effacing in terms of their own health outcomes (Miniszewska et al., 2013b), and use more positive, adaptive strategies for coping with their psoriasis (Fortune et al., 2002; Ograczyk et al., 2014; Scharloo et al., 2000; Wahl et al., 1999), tend to view psoriasis as less burdensome on their lives. In contrast, viewing psoriasis as something that should be controllable or curable, and as something that has disabling consequences, has been related to a more negative perception of health overall (Scharloo et al., 2000). The amount of social support a person has available to them is also important, with greater social support related to higher life quality in people with psoriasis (Janowski et al., 2012; Scharloo et al., 2000), particularly in women (Janowski et al., 2012).

Findings of other studies support the passing of time as a factor in adjusting to psoriasis (Unaeze, Nijsten, Murphy, Ravichandran, & Stern, 2006; Uttjek et al., 2007; Watson & de Bruin, 2007). The chronicity of psoriasis means that people live with the disease over many years, usually decades, and sometimes over a lifetime, depending on their age at the time of onset. Therefore, psoriasis is typically present throughout many different life stages, and as people's experience of life changes, so too may their experience of psoriasis. The majority of research that has been conducted into the experience of psoriasis is limited in that it has been based on how people live with psoriasis in the present, and given little, if any insight into how this may have evolved over time. The few studies that have involved time in their analyses in

any meaningful way have offered differing perspectives on how the experience of psoriasis can change over the longer-term. An 11-year follow-up on a quantitative assessment of quality of life suggested that over time, people begin to worry less about their physical appearance and what others might think of them, and feel less embarrassment and shame (Unaeze et al., 2006), sentiments that were echoed in interviews about the daily experience of psoriasis (Uttjek et al., 2007). In the latter study, participants linked their ability to adjust to psoriasis to the routines around treatments and behaviour that they had established over time, as well as to viewing their own situation favourably compared to that of others (Uttjek et al., 2007). In another study that explored the impact of psoriasis on self-concept, participants' struggles with psoriasis ultimately motivated them to seek a better way to live with the disease, and this led to fundamental personal changes over time such as the development of greater strength and resilience (Watson & de Bruin, 2007). The findings of this study suggested that having a positive disposition and self-concept prior to the onset of psoriasis allowed participants to be able to positively transform their difficult experiences with psoriasis over time, which is supported by findings that related a positive, optimistic outlook on life to better adjustment to and acceptance of psoriasis (Zalewska, Miniszewska, Chodkiewicz, & Narbutt, 2007).

In contrast, others have offered evidence that the impairment arising from psoriasis can be cumulative over the course of a person's life, particularly in those with more severe psoriasis, even if psoriasis later becomes well-controlled and is seen as having no impact on quality of life in the present (Warren et al., 2011). The notion of a cumulative burden describes how having a condition such as psoriasis might permanently and adversely alter the course of a person's life from the path it could otherwise have followed (Kimball et al., 2010). Using evidence from four case studies, the authors gave support to this notion by illustrating how having psoriasis had been paramount in preventing participants from achieving life goals, pursuing their preferred career, gaining their optimal level of education, developing social relationships, gaining full pleasure from family life or having children (Warren et al., 2011).

Most of these studies emphasise that the approach people take towards living with psoriasis, such as the coping strategies they use, as well as their overall disposition, sense of self and outlook on life can be highly influential in whether people are able to adjust to life with the disease. Even so, it has been suggested that impairment from the impact of more extensive psoriasis over time may adversely influence the direction that a person's life takes, even if they feel they have adjusted to their psoriasis.

3.1.8. Conclusion

This section has discussed how the experience of living with psoriasis is typically a negative one, with its implications widespread across essentially every area of life. Central to this negativity are feelings of embarrassment, shame and stigmatisation arising from the appearance of psoriasis, which contribute to low self-confidence and self-esteem, and impaired body- and self-image. Social and intimate relationships, fulfillment in career and educational pursuits and a willingness to participate in normal, everyday activities can all be greatly hindered as a result of having psoriasis. Furthermore, physical symptoms such as itch, flaking skin and pain, and the lack of satisfaction with available treatments and their inconveniences and side effects can further contribute to the strain of living with psoriasis. Not only do these factors negatively impact a person's social and emotional wellbeing, but they can also be compounded by a lack of understanding about psoriasis from others. That people with psoriasis commonly experience stigmatisation and lack of understanding towards psoriasis from the lay public, and even members of the health profession, suggests that there is a need for further insight into what the experience of psoriasis is like for those who suffer from it. Because people's experiences of living with psoriasis and the factors that influence them are unique to individuals, this area of research will benefit from more studies using a qualitative approach, as such research can consider the subtleties and connections in people's experiences that are often overlooked with quantitative methods. Thus, the first major aim of this thesis is to gain new insights into what it is like to live with psoriasis, through understanding the narrative forms that people use to make sense of their experience.

In order to demonstrate how new understandings relating to the experience of psoriasis can be gained through taking a narrative approach, this thesis will now turn to the methodological considerations of this research, beginning with an introduction to epistemological perspectives and a critical discussion of the methodological approaches that have previously been used to understand the experience of psoriasis.

3.2. Methodology

The methodology of narrative inquiry was employed for this research because studying people's narratives provides a rich opportunity for understanding how they experience and make sense of their psoriasis (Kleinman, 1988). This methodology will be elaborated on further below, but firstly, the epistemological perspective from which this research is conducted will be described. Engaging with any methodology involves certain assumptions, and some of the most fundamental of these assumptions are concerned with how we can understand what we know, or alternatively stated, where meaning comes from. This is known as an epistemological perspective (Willig, 2012). In order to have a good understanding of what kind of knowledge can be derived from using a narrative inquiry methodology, it is first important to clarify the epistemological perspective that it is informed by (Chamberlain, 2015a), which in this case is that of social constructionism. Thus, this section begins with a brief overview of different epistemological positions. Following this is a discussion of the methodological approaches that have previously been used to understand the experience of living with psoriasis. The focus then shifts to providing an explanation of social constructionism, in order to set out the epistemological underpinnings of the original research in the following chapter. This is followed by an explanation of narrative inquiry, and why it is a useful methodology in light of the research question. This leads into a description of the participants who took part, the methods that were used, and the process of analysis that was engaged with in order to make sense of the data.

3.2.1. Epistemological perspective

In so-called 'traditional' scientific enquiry, such as that based on the scientific method, there tends not to be explicit presentation of the researcher's epistemological position. It is not that such a position does not exist, because accompanying all research is a powerful set of underlying assumptions, but that these tend to be taken for granted in traditional scientific research (Crotty, 1998; Willig, 2012). Such research is informed by an objectivist epistemological position, which assumes that meaning, or 'truth', is to be found in objects and phenomena themselves (Crotty, 1998). The theory of positivism, from which the scientific method arose, states this 'truth' to be discoverable, and therefore, the outcomes of this kind of research, by supporting a hypothesis or not, are thought to enlighten us further to what is (or equally, what is not), and so to bring us closer to knowing the 'truth' (Moghaddam, 2005). Perhaps due to the long tradition and relative dominance of positivist research, this epistemological perspective has been widely adopted in Western society, with the positivist notion of 'cause and effect' needing no introduction or justification.

In qualitative research in the human and social sciences, however, there is a need for explicitly stated epistemological assumptions (Chamberlain, 2015a). Without first understanding one's epistemological perspective, it is difficult to make full sense of data, or even to identify the best methods by which to approach research (Crotty, 1998). Qualitative research is concerned with describing, with understanding, with finding meaning (Willig, 2012), and therefore, the 'lens' through which such research is undertaken must be explicitly described. For example, in conducting research and presenting the findings, it must be clarified whether the results are deemed to arise from the object or phenomena being studied, or from the person conducting the study, or through a complex interaction between the two. The distinction between each of these 'lenses' means that the choice of which to use profoundly alters the meaning and interpretation of the results (Willig, 2012). Thus, especially in qualitative research, it is immensely important to clarify one's epistemological perspective, as it is a consistent foundation that informs the meaning of the research in its entirety.

I have already briefly introduced one epistemological position, objectivism. This position is taken up in the second half of this thesis, which takes a positivist approach to investigate the impact of vitamin D on psoriasis. A second, less common perspective, is subjectivism. Directly contrasting with objectivism, subjectivism espouses that meaning is solely located in the human being, who imposes self-derived meaning on objects or phenomena (Crotty, 1998). A third, contrasting epistemological perspective is social constructionism, which holds that meaning does not arise from objects, or from within people, but is constructed through the interactions of people with the world around them (Crotty, 1998). Social constructionism therefore places emphasis on the social and cultural context for understanding how people make sense of and experience phenomena (Moghaddam, 2005), and it is this from this perspective that the research in the first half of this thesis is conducted. A more detailed understanding of the concept of social constructionism will be presented in Section 3.2.2., but this chapter will first turn to a discussion of the methodological approaches that have been previously taken with regards to understanding the experience of psoriasis, in order to ultimately justify why a narrative inquiry approach from a social constructionist perspective has been adopted for the current research.

3.2.2. Methodological approaches of past research into the experience of psoriasis

The vast majority of studies that relate to the experience of psoriasis have been conducted from an objectivist epistemological perspective, with much of this research conducted using quantitative methods such as closed-ended questionnaires or surveys (e.g., Anstey et al., 2012; Boehm et al., 2013; Bronsard et al., 2010; Nash et al., 2015). This type of research has value in that it can provide an indication of measurable factors, such as the prevalence of issues relating to psoriasis, and the relative extent to which the average person with psoriasis considers them to be a burden. However, this type of research does not offer insight into *how* people experience psoriasis. For example, an item from the Dermatology Life Quality Index questionnaire: “Over the last week, how much has your skin affected any social or leisure activities?” (Finlay & Khan, 1994) may be answered in the same way (‘very much’, ‘a lot’, ‘a little’, ‘not at all’, or

‘not relevant’) by two different people, yet the way in which each person experiences an impact of psoriasis on social and leisure activities might be very different. Similarly, psoriasis leads to embarrassment in many people (Sampogna et al., 2012), but feeling embarrassed in relation to psoriasis might mean different things to different people, and it might arise for different reasons.

A smaller body of qualitative research has been conducted into the experience of psoriasis from the perspective of the sufferer. As qualitative research is focused on gaining insight into how people understand their world and make sense of their experiences (Willig, 2013), the methods that have been used in these studies have been centered around allowing new understandings of participants’ experience of psoriasis to emerge. Previous research into the experience of psoriasis has been based on various epistemologies (not usually made explicit), and can also be considered in relation to the methodological approach and methods that were used, the depth of understanding and insight it offers into the experience of psoriasis, and to the degree of interpretation that was involved in determining the findings (Braun & Clarke, 2006). The discussion in this section is centred on the methodological approaches of a range of qualitative research that has focused on understanding people’s experiences with psoriasis beyond the categorisation of findings under pre-determined themes (e.g., physical impact, psychological impact). Studies that have taken the latter approach offer comparable findings to quantitative studies, capturing little that is new in terms of understanding the experience of psoriasis. (Note: early research of this nature, e.g., Campbell, Warburton, Amos, & Roland, 1996; Jowett & Ryan, 1985, was of importance at the time due to the scarcity of research illustrating the significant impact of psoriasis from the perspective of the sufferer). Research studies that have taken a qualitative approach towards understanding the experience of psoriasis and are included in this discussion are presented in **Table 3**.

Most qualitative research into the experience of psoriasis has been conducted using face-to-face, semi-structured interviews. In this type of interview, the researcher asks selected, open-ended questions to ensure the particular areas of interest are covered, and the participant is encouraged to answer at length. This style of interview allows participants to elaborate on aspects that are

important to them, and enables the researcher to explore new ideas that arise, meaning an in-depth understanding of people's experience can be sought. One study, which aimed to identify factors of importance in relation to the management of psoriasis, combined semi-structured interviews with an ethnographic approach, which involved a researcher observing participants as they went about their normal activities, and documenting their behaviours with video and photographs (Bewley et al., 2014). The benefit of such an approach was being able to gain insight into the lived, day-to-day experience of participants; the researchers then interpreted the meaning of aspects of this experience, with enhanced understanding derived from participants' perspectives through interviews.

In other studies, more unusual approaches were used to gain an understanding of people's personal models of psoriasis (Bundy et al., 2014) and the experiences of adolescents (aged 11 – 18 years) with psoriasis (Fox, Rumsey, & Morris, 2007), respectively. In the first study, participants were invited to complete a postcard that was addressed "Dear Psoriasis", but was otherwise blank (Bundy et al., 2014). The 'blank slate' approach meant that respondents shared a wide range of different insights and thereby a broad spectrum of experience. On the other hand, the brief nature of responses limited the amount of detail that could be provided in terms of the consequences of psoriasis and personal experience. The second study used a closed online forum in which a researcher was present to stimulate discussion between young people about their experiences of psoriasis (Fox et al., 2007). This format was chosen due to the perceived difficulties of recruiting people of that age group to attend and openly participate in face-to-face interviews about what were likely to be sensitive issues (Fox et al., 2007). In contrast, the anonymity of the online forum meant most participants seemed to be more comfortable sharing their experiences, and this was likely enhanced by the 'online chat' format, which was probably very familiar to them. Similarly, respondents in the postcard study were able to remain anonymous, perhaps encouraging more open sharing; on the other hand, the style of response meant that participant characteristics could not be captured, prohibiting an understanding of the background of those who offered their views.

Table 3. Previous research using a qualitative approach to understand the experience of psoriasis

Author (year)	Aim(s)	Participants	Methods	Methodological approach
Ghorbanibirgani et al. (2016)	To describe and explain the social stigma and rejection experienced by patients with psoriasis.	15 adults referred to a hospital dermatology ward/clinic (Iran)	Semi-structured interviews	Thematic analysis informed by hermeneutic phenomenology
Khoury et al. (2014)	To investigate the influence of psoriasis on patients' body image.	8 adults with moderate to severe psoriasis (Denmark)	Semi-structured interviews	Thematic analysis
Bewley et al. (2014)	To identify the relative importance of factors related to effective management of psoriasis for patients.	56 adults with various psoriasis severities (UK, other countries in Europe and North America)	Observation of participants in their own homes over 4 – 8 hours; semi-structured interviews	Ethnography with thematic analysis
Bundy et al. (2014)	To gain a better understanding of people's experiences living with psoriasis using a novel method of data collection.	104 members of the Psoriasis Association (UK)	Participants completed an anonymous postcard addressed 'Dear Psoriasis...'	Thematic analysis with a modified grounded theory approach
Nelson et al. (2013b)	To explore perspectives of people living with psoriasis including coping responses, self-care strategies and how consultations with healthcare professionals are experienced.	29 adults with psoriasis (UK)	Semi-structured interviews	Thematic analysis
Warren et al. (2011)	To deepen understanding of the impact of psoriasis across the life course by exploring causes and mechanisms of impairment, along with moderating factors.	4 adult patients with long-term experience of moderate to severe psoriasis as representative cases (UK)	Construction of case studies from patients' narratives (further detail not given)	Analysis of case studies in context of theory
Magin et al. (2011)	To explore the notion of 'perfect skin' in relation to the psychological co-morbidities of psoriasis.	29 adults with a range of psoriasis severities from general practice and dermatology clinics (Australia)	Semi-structured interviews	Thematic analysis with a modified grounded theory approach

Continued on next page

Errser et al. (2010)	To explore how adults with psoriasis self-manage their condition and to identify strategies that can help people self-manage effectively.	22 adult general practice patients using only topical therapies	Focus groups	Thematic analysis
Magin et al. (2010)	To explore the effects of psoriasis on sexual functioning and sexual relationships.	29 adults with a range of psoriasis severities from general practice and dermatology clinics (Australia)	Semi-structured interviews	Thematic analysis with a modified grounded theory approach
Magin et al. (2009a)	To explore the psychological co-morbidities of psoriasis.	29 adults with a range of psoriasis severities from general practice and dermatology clinics (Australia)	Semi-structured interviews	Thematic analysis with a modified grounded theory approach
Magin et al. (2009b)	To explore the experiences of patients with psoriasis in relationships with their treating doctors.	29 adults with a range of psoriasis severities from general practice and dermatology clinics (Australia)	Semi-structured interviews	Thematic analysis with a modified grounded theory approach
Magin et al. (2008)	To explore the experiences of teasing and bullying in patients with psoriasis, and the role of appearance-related teasing and bullying as mediators of psychological morbidity.	29 adults with a range of psoriasis severities from general practice and dermatology clinics (Australia)	Semi-structured interviews	Thematic analysis with a modified grounded theory approach
Fox et al. (2007)	To explore the experiences of young people with chronic skin conditions to identify their needs for support.	8 young people with psoriasis (11 – 18 years) (UK)	Focus groups via an anonymous online forum	Grounded theory analysis
Uttjek et al. (2007)	To find out how psoriasis can affect the individual's everyday life, and if there are any differences between genders.	18 adults with psoriasis (Sweden)	Semi-structured interviews	Qualitative content analysis

Continued on next page

<p>Watson & de Bruin (2007)</p>	<p>To describe the lived experience of people with psoriasis and the impact of psoriasis on their concept of self.</p>	<p>7 adults with psoriasis (South Africa)</p>	<p>Semi-structured interviews</p>	<p>Existential phenomenology</p>
<p>Wahl et al. (2002)</p>	<p>To study patients' lived experience of psoriasis to identify different aspects of the burden of living with psoriasis.</p>	<p>22 adults with severe psoriasis (Norway)</p>	<p>Semi-structured interviews</p>	<p>Grounded theory analysis</p>

Analysis of findings from qualitative studies into the experience of psoriasis has involved various methods of interpretation to gain greater understanding of a specific aspect of experience, or the experience overall. For example, some research has involved close analysis of the collected data to identify the major themes of importance in relation to the experience of psoriasis. Types of thematic or content analysis were used to understand people's personal models of psoriasis (Bundy et al, 2014), the influence of psoriasis on body image (Khoury et al., 2014), the experience of social stigma and rejection (Ghorbanibirgani, Fallahi-Khoshknab, Zarea, & Abedi, 2016), the effect of psoriasis on daily life (Uttjek et al., 2007) and issues relating to treatment and care of psoriasis (Bewley et al., 2014; Ersser et al., 2010; Nelson et al., 2013b). In conducting such analysis, researchers reported that they first immersed themselves in the data, then identified dominant themes based on their frequency across the sample and/or the strength of a single response. In some cases, the analytic process was inspired by the method of grounded theory, in that it involved constant comparison between the main ideas that were identified and the rest of the data, to ensure the findings were representative of the data overall and to capture any nuances (Bundy et al., 2014; Khoury et al., 2014; Nelson et al., 2013b; Uttjek et al., 2007). Some researchers took this analysis to the next level by identifying relationships between themes, and grouping subthemes under broader themes (Khoury et al., 2014; Nelson et al., 2013b), giving greater insight by providing a representation of the relationships between different parts of experience. For example, in the study on body image in psoriasis, the sub-theme "the struggle for an ideal appearance" was organised under the theme of "body coverage", illustrating that this struggle relates to the need to hide psoriasis from others (Khoury et al., 2014, p. 4).

Using a slightly different approach, Uttjek et al. (2007) placed emphasis on the influence of participants' personal characteristics such as age, age at onset, gender and living area in their content analysis of the effect of psoriasis on daily life. While the themes they presented (marked by visibility, joint changes, adjustment, routinisation, quality of life) seemed somewhat misaligned with their goal of describing the effect of psoriasis on daily life, consideration of

factors such as the length of time living with psoriasis meant that the meaning of psoriasis for participants over time was included within the discussion of themes. The use of thematic or content analysis has therefore allowed identification of salient aspects of the psoriasis experience in relation to the researcher's specific area of interest. At this basic level, the level of interpretation by researchers is minimal, with the level of insight offered into the experience increasing alongside the degree of interpretation (i.e., with the identification of relationships between concepts and factors influencing experience).

In some research, the choice of methodology and method has allowed the development of an overall schema or conceptual framework to theoretically represent the experience of psoriasis. Such research has been based on various versions of grounded theory methodology, the purpose of which, as the name suggests, is to develop new theories that are based on, or 'grounded in' the data. This approach has been used to develop a schema of the psychosocial experience of psoriasis (Magin et al., 2009a), and to understand the experiences of people with severe psoriasis (Wahl et al., 2002) and adolescents with psoriasis (Fox et al., 2007). Unlike many of the studies using thematic or content analysis, the identification of relationships between aspects of experience was central to the findings of research conducted using grounded theory. For example, through attending to connections between concepts from participants' interviews, Magin et al. (2009a) claimed that the appearance of psoriasis was at least one of the factors central to the psychological morbidity arising from psoriasis. They also identified numerous factors that appeared to affect this relationship, and thus the overall experience of psoriasis. While these factors were described at a simple level in the original research, more in-depth analyses of some aspects (experiences of teasing and bullying, the idea of 'perfect skin', the impact on sexuality), including the identification of sub-themes, were presented as separate research papers, allowing for more in-depth exploration of these specific areas to also be presented (Magin et al., 2011; Magin et al., 2008; Magin et al., 2010). Wahl et al. (2002) also identified the relationships between aspects of the psoriasis experience using a grounded theory approach. They identified 'bodily suffering' to be at the core of the experience of severe

psoriasis, with the degree of this suffering influencing the extent to which other sub-categories (the visible body, social vulnerability, staying on an even keel, and psoriasis as an all-consuming disease) were experienced. Further, this model demonstrated how experiences relating to these different sub-categories interacted with and intensified each other (Wahl et al., 2002).

One other study using a grounded theory approach was the investigation into the experience of adolescents with psoriasis mentioned earlier (Fox et al., 2007). The use of an online forum meant that analysis could involve an exploration not only of the experiences of individuals, but how people related to one another in the context of their common experience of psoriasis. Consequently, the conceptual framework that was derived from this analysis consisted of three categories: the first ('It and Me – the struggle') captured the interactions that occurred between people and their psoriasis; the second ('It and Us') illustrated the sense of shared experiences and identity that arose between participants in opposition to their psoriasis, and the third ('Us and Them'), the relationship between 'people with psoriasis' as a group and others who do not have the condition (Fox et al., 2007). These findings highlighted the ongoing struggle the young people faced in living with psoriasis, the sense of difference and separateness from others that they felt because of their skin, and the benefit that arose from being able to connect with others who had been through similar experiences. Research conducted into the experience of psoriasis using a grounded theory approach has therefore provided considerably more than a static description of the overall experience, but rather has offered dynamic representations of how the different elements of experience can shift and interact with each other to form the experience overall, and how people's experiences may be influenced through their interactions with others.

Different forms of phenomenology have informed the methodological approach of other studies aimed at gaining a rich understanding of how people experience psoriasis. Broadly speaking, phenomenology relates to how people experience things (i.e., 'phenomena'). In research that aimed to understand the lived experience of social stigma and rejection in people with psoriasis

in Iran (Ghorbanibirgani et al., 2016), the philosophy of hermeneutic phenomenology underpinned thematic analysis, and therefore how themes were interpreted. This meant that researchers placed emphasis on the subjective experience of participants, and thus, the meanings derived from people's interpretations of their experiences relating to social stigma and rejection. Each theme offered insight into how participants perceived the experience of psoriasis in relation to these aspects, and showed that they experienced a lack of social support, being given unrealistic and inappropriate labels, rejection and isolation, and feelings of absurdity and futility (Ghorbanibirgani et al., 2016). In this study, however, there was little interpretation of experience beyond the identification of common themes among participants, with descriptions of themes heavily reliant on participants' quotes. The findings therefore illustrate some of the issues faced by people with psoriasis (in this case, specifically in social settings in Iran), but limited insight into the way in which these issues are experienced.

Another form of phenomenology, existential phenomenology, is concerned with how people deal with the fundamental aspects of existence (such as illness, death, isolation, responsibility etc.), how they interpret and give meaning to these experiences, to the self, to others, and to the world, and how the experiences then affect the person's sense of reality (Watson & de Bruin, 2007). From this perspective, Watson and de Bruin (2007) sought to gain deep insight into the essence of the lived experience of psoriasis and how it impacts the self-concept of sufferers. Their process of analysis involved the researchers 'bracketing' previously held assumptions about the experience of psoriasis in order to consider how participants might have experienced it at the foremost level of consciousness. Four broad existential issues were identified in relation to the impact on the self-concept: the impact of psoriasis, the impact of its treatments, the impact of the doctor/patient relationship, and coping methods that enhanced the self-concept. Using participants' descriptions of their experiences, researchers constructed a representation of how they experienced events first as individuals, then as a group, and the final analysis involved a representation of the experience of psoriasis in relation to its influence on the self-concept under the four broad issues (Watson & de Bruin, 2007). This analysis involved

a significant degree of interpretation on behalf of the researchers, who sought to understand not just how people experienced psoriasis, but what it meant for them in relation to their sense of self and how this changed over time. This was also one of the few studies to consider how the experience of psoriasis changes over time, and thus to present the experience of psoriasis as a kind of unfolding story.

In another study that included the consideration of time, researchers aimed to gain a deeper understanding of the ways in which psoriasis can influence people's overall life course through the impairment that it is seen to cause (Warren et al., 2011). Analysis was conducted on four case studies constructed from participants' narratives, and involved a straightforward identification of links between aspects of psoriasis such as disease course and treatment use, the negative implications of psoriasis (e.g., stigmatisation or limited employment opportunities), and the long-term impairment that had occurred as a result of these factors (Warren et al., 2011). While this research offered examples of what the researchers considered to be 'typical' examples of living with psoriasis over the long-term in people with moderate-to-severe disease, this study was about identifying factors perceived to be involved in impairment over time, and not about gaining a deeper understanding of experience, *per se*.

This section of the chapter has so far discussed the various methodological approaches that have been taken towards understanding the experience of psoriasis. Across the body of research addressing this area, relatively few studies have focused on gaining understanding of the overall experience at an in-depth level. Of those that have, most have involved analysis limited to identifying common or important themes across the data, which provide an understanding of factors relating to the experience of psoriasis, yet have not often included much interpretation of what these factors mean in the context of people's lives. Furthermore, this type of analysis does not provide insight into how the experience of psoriasis can shift and evolve in response to various other influences and circumstances. Conceptual frameworks constructed using grounded theory provide a more dynamic understanding of experience, but have been focused on specific aspects of psoriasis experience (i.e., psychological morbidity), or limited to

particular groups of people (i.e., adolescents and those with severe psoriasis). Further, this type of research does not give insight into how the experience of psoriasis might evolve and change over time. On the other hand, one of the studies that took a phenomenological approach towards understanding the lived experience of psoriasis did illuminate the experience of psoriasis over time, yet it was considered specifically in terms of how psoriasis and its related factors affect people's self-concept. Similarly, case studies offered 'stories' of psoriasis over time, but analysis was focused solely on impairment and its contributing factors.

One other type of qualitative approach, narrative inquiry, offers a different means by which the experience of psoriasis can be understood. This approach is based on the premise that human beings are storytellers by nature, and therefore understand life in storied form (Sarbin, 1986; Smith & Sparkes, 2006). As Bruner argues, people do not make sense of each aspect of their lives, and each event that occurs, on a one-by-one basis, but instead, frame them according to larger, underlying structures (or forms) that provide context for understanding the meaning of the experiences they encompass (Bruner, 1990). It follows, then, that understanding the narrative forms that people use when they talk about their psoriasis gives insight into the meanings that they ascribe to their psoriasis-related experiences (Riessman, 2008). Furthermore, just as illnesses do not occur in isolation from a person's wider life circumstances, narratives consider the experience of illness within the context of people's lives, which are themselves situated within a specific cultural, environmental and temporal context (Kleinman, 1988). Narrative analysis has become widely accepted as useful for understanding experiences of illness, and a case has even been argued for the importance of understanding the narratives of people with psoriasis in order for their doctors to be able to provide them with better care (Kennedy, 2006). The researcher who put forth this argument conducted three semi-structured interviews in which people were encouraged to share their experiences at length, yet analysis of these narratives was limited to identification of major themes, and thus, was essentially thematic analysis (Kennedy, 2006). However, narrative analysis can be conducted at a deeper level, by considering not only the content of narratives but also their underlying forms, as these give

greater insight into how people shape and understand their experiences. Analysis of narrative forms has offered rich insight into the experiences of people with numerous other illnesses and disabilities (e.g., Day & Wadey, 2016; Ezzy, 2000; France, Hunt, Dow, & Wyke, 2013; Miconi, De Nuzzo, Vatne, & Pierantognetti, 2015; Mitchell, Skirton, & Monrouxe, 2011), but such an approach has not yet been taken in relation to understanding the experience of psoriasis.

Having justified the potential for new insights into the experience of psoriasis to be gained through narrative analysis, this chapter will provide a more detailed explanation of narrative and how it relates to the experience of illness. Firstly, however, greater clarification will be given around the epistemological position that narrative analysis is informed by, that being social constructionism. As it is impossible to separate narrative analysis from its social constructionist underpinnings, it is important to understand this position before turning to the greater detail of narrative.

3.2.3. Definition of social constructionism

Social constructionists view meaning as arising not from objects themselves, or from people, but as constructed in the interaction between human beings and the world around them (Crotty, 1998). From this perspective, therefore, it is to this interaction, this engagement of humans with the world, that we must look in order to understand and find meaning in human experience. It is important to note here the distinction between the construction of meaning versus the creation of meaning (which is subjectivism) or the discovery of meaning (objectivism) (Crotty, 1998); from a social constructionist perspective, meaning does not emerge as something from nothing, nor is it found someplace. Rather, meaning is constructed from what is there already, that is, what the object offers the person, and what the person brings to the object (Crotty, 1998). Thus, both the person and the object or phenomena are vital players in the construction of meaning.

The concept of intentionality is helpful in illustrating the interaction between humans and their environment that forms the basis of social constructionist thought. However we as humans are, we are with intention towards something. 'Intention', used in this sense, refers to the sense of

‘directing oneself to’, and as Crotty explains, “consciousness...is always consciousness of something” (Crotty, 1998, p. 44). Humans are, by nature, responders, and the way we respond to things, either consciously or subconsciously, helps us to create meaning from them, whether acknowledged or not. Therefore, it is important that people are not considered in isolation from their environment or experiences, but on the contrary, that these aspects are seen as important partners in the meaning-making process.

The ‘social’ aspect of social constructionism emphasises the centrality of the historical, social and cultural context to the generation of meaning (Crotty, 1998). As mentioned above, human beings do not make sense of things in their world on their own, one by one, constructing new and unique meanings with every encounter (Bruner, 1990; Crotty, 1998). Instead, we are born into an already established ‘world of meaning’, which shapes the way we experience phenomena (Bruner, 1990; Crotty, 1998). For example, when we encounter a flat, smooth, white rectangular object made out of dried wood pulp, we generally overlook these physical characteristics and go straight to our understanding of it as a piece of paper. We are viewing it through a particular cultural lens, one that leads us to unquestionably accept the ‘fact’ that this is a piece of paper, and that a piece of paper is endowed with certain qualities and is used for certain purposes. From a social constructionist perspective, however, there are no ‘facts’, but instead, there are ways of seeing things, and these ways differ according to cultural and social contexts. This can be understood by considering that the same flat, smooth rectangular object is accorded different titles and functions depending on when, where and by whom it is being engaged with. A remote group of tribes people, for instance, are likely to name and view such a thing quite differently to, say, a group of poets; for whom it would hold a different meaning again to, say, those in the printing industry. Similarly, the historical context matters (Burr, 2015; Crotty, 1998; Moghaddam, 2005). For example, paper may have been imbued with different meanings when it was a relatively new invention, compared to now, when it has existed for millennia; and if paper were to become scarce tomorrow, it would likely take on different meaning to that of today, being a time of abundance. Hopefully these examples make

it clear that from a social constructionist perspective, meaning is not to be found, nor is it fixed or universal, but that it is through the use of shared meanings, which are dependent on culture, that humans interpret and make sense of the world. We learn how to see things and understand them, and in fact, we also learn what not to see (Crotty, 1998). In this way, the objects and meanings that people deem to be important come to the fore. Through this process, we form a 'social reality' in which meanings are "constructed, sustained and reproduced through social life" (Crotty, 1998, p. 55).

It follows, then, that social constructionists reject the concept of an objective truth that can be sought and identified (Burr, 2015; Moghaddam, 2005). Instead, they embrace the potential for an infinite number of 'truths', which are based on the meanings a person constructs in response to their world – yet always in relation to their specific cultural and social context. Such 'truths' are not bounded or determinate, but are instead malleable and changeable, as they depend not only on circumstances, culture and context, but also on happenings and change in the person themselves (Burr, 2015). It goes without saying that between humans, even those from the same cultural setting, the type of response to the same thing can differ tremendously; thus, so can the meaning of that thing to each person. Yet they are no less valid because of their plurality and apparent fickleness, as they hold meaning for someone, and that is what is of greatest importance here.

3.2.4. Narrative

Narrative has its origins in literary traditions; however, the use of narrative now pervades almost every discipline (Riessman, 1993), with variations on its use and interpretation. Possibly due to this ubiquitous application, there is no one definition of narrative. In the context of narrative inquiry, a form of research focused on how stories are used to describe human action and experience (Polkinghorne, 1995), narratives are generally thought of as stories or structures in which people order events, actions and other aspects of life and relate them over time in such a way as to attribute meaning to such experiences (Bruner, 1990; Hyden, 1997; Polkinghorne,

1995; Stephens & Breheny, 2013). In fact, narratives can be seen as the means or the “vehicles” by which people make sense of their lives (Blaxter, 2004, p. 170), capturing how people view their lives and selves according to narratives, with everything they think, perceive, imagine and base their moral decision-making on deriving from the narrative structures they create (Sarbin, 1986). The research presented in this part of the thesis takes up these positions, viewing narratives as the way through which people construct and link different aspects of their lives to create coherent and meaningful stories, thereby enabling them to make sense of these aspects and their lives overall. These ideas and the concept of narrative will be elaborated on in the following sections.

Characteristics of narratives

Narratives have certain features that distinguish them from other bound sequences of written or spoken text. Firstly, narratives are concerned with human action, with “human attempts to progress to a solution, clarification, or unraveling of an incomplete situation” (Polkinghorne, 1995, p. 7). Alongside actions, literary theorist Kenneth Burke proposed four other elements that are central to well-formed stories: when or where the act took place (the scene), who did it (the agent), how he or she did it (agency) and why (the goal or purpose) (Burke, 1969, p. xv). An imbalance between any of these five primary elements motivates the action, in the sense that the imbalance must be dealt with in order for the goal of the narrative to be achieved (Bruner, 1990). For example, in people with psoriasis, the goal of their narrative might be to overcome their psoriasis, yet an imbalance occurs if they have no means (i.e., agency) by which to do so. Thus, their narrative is motivated by their efforts to find a way to overcome psoriasis.

With those elements in place, we can now turn to a critical concept of narrative: what has been referred to as both sequentiality (Bruner, 1990) and contingency (Salmon & Riessman, 2008), but what is possibly best understood as a combination of the two. The events, actions, mental states and thoughts that occur throughout human lives are not seen as holding meaning in themselves; rather, people bestow them with meaning by ordering them within an overall storyline or plot (Bruner, 1990) and linking them with each other in a consequential manner

(Salmon & Riessman, 2008). Polkinghorne offers a useful comparison for this process of meaning-making through the formation of a plot: “Emplotment composes meaning out of events by a process similar to the process that grammar employs to develop meaning from words” (Polkinghorne, 1988, p. 159). The storyline or plot that the teller constructs is therefore the “life-blood” of the narrative (Riessman, 2008, p. 4), illuminating the significance of individual constituents for each other and for the overall plot, and thus the meaning that is given to them by the teller.

Underlying storylines are specific narrative forms, or “the most general storyline[s] that can be recognised underlying the plot and tensions” of stories (Frank, 2013, p. 75), and as people’s stories are usually complex, they involve the interweaving of many different narrative forms that shift and change over time (Frank, 2013). Basic examples of narrative forms include the comedy and the tragedy, in which the protagonist does or does not achieve their goal, respectively (Polkinghorne, 1995). However, the array of narrative forms is wide, and includes those that have been specifically identified in stories of illness (as discussed below). The complexity of people’s stories means that being able to identify the narrative forms they use when telling them is an important part of the listening process, as this allows the meaning of even the most complicated stories to be better understood (Frank, 2013).

A starting point from which to understand the narrative form of a story is to identify the goal or outcome that the story moves towards (Polkinghorne, 1995). The goal shapes the manner in which happenings are woven into the narrative, as the story is told in such a way to support the achievement of the goal (Hyden, 1997). As part of this, the narrative’s sense of directionality can be understood, as the narrative can move either away from or towards the goal as it moves from one event to the next (Polkinghorne, 1995). While the concept of a goal might be straightforward in narratives with one distinct storyline, this concept should be clarified in relation to personal narratives, which are extended accounts of people’s lives in their wider context that are developed through interaction with another person over the course of interviews or conversations (Riessman, 2008). The goal of a personal narrative told at any one point in

time should not be considered as finite, for so long as a person is alive (and in many cases, for some time after their passing), their story will continue (Frank, 2010; Polkinghorne, 1995). In this context, therefore, the ‘goal’ of the narrative should be understood as the point that is desired or reached at the time that the narrative is constructed, but that has the capacity to shift as time continues.

3.2.5. Narrative and social constructionism

From the account of narrative given above, then, it may be apparent that social constructionism is relevant to the concept of narrative in every way. Narratives are seen as constructions of reality, the most fundamental tenet of social constructionism (Crotty, 1998), rather than as reflections of a ‘true reality’ (Wertz et al., 2011). Thus, narrative as a concept supports the potential for the construction of multiple versions of ‘truth’, in that a narrative is always one of many possible narratives about the same situation or life (Riessman, 1993; Wertz et al., 2011). The construction of one particular narrative over another is influenced by the specific social, cultural and historical context within which the narrative is constructed (Polkinghorne, 1995), with the meaning of a person’s experiences arising from the way they understand and interact with the world around them. Furthermore, people draw from already-established shared social and cultural narratives in order to make sense of their experiences (Bruner, 1990). Therefore, on one level, to understand people’s experiences through narrative inquiry underpinned by a social constructionist epistemology means to examine the ways in which people currently understand their world, inherent within which are meanings specific to the particular time and circumstances in which they live.

On another level, the social constructionist assumptions underpinning narrative inquiry mean that the way that people talk about their experiences, and thus the narratives they use, cannot be considered in isolation from who they are telling them to and for what purpose (Hyden, 1997). Instead, the narrative is seen as being jointly constructed by both the participant and the researcher, with the researcher playing an active role in shaping how a person goes about telling

his or her story (Mishler, 1986; Riessman, 2008). Construction of a story for a particular audience and setting involves a person placing emphasis on certain aspects of their experience that they deem to be important to their story in that particular context, bringing these aspects to the foreground, while minimising or omitting others. Thus, the narrative that arises from the interaction between a participant and a researcher will likely differ from the one a person might share in conversation with, for example, a medical doctor, or a close friend (Hyden, 1997). Not only do the researcher's specific questions and utterances influence a participant's responses, but the participant also learns what type of response to give, such as whether to offer a long, elaborate description or a brief, surface-level response, by the way the researcher asks questions or reacts to their answers (Mishler, 1986).

Furthermore, a social constructionist perspective expounds that the meaning of a narrative, and thus of a person's experiences, does not arise from the narrative itself, but through the process of engaging with it and interpreting it within a certain context. Therefore, in the research setting, the researcher's interpretation of the narrative is yet another level at which meaning is constructed. In interpreting the meaning of a narrative, a researcher must give weight to the overall context in which it is situated, including the social, cultural and historical circumstances and the meanings that are found within these contexts, and consider how these influence the narrative a person tells (Polkinghorne, 1995). Just as a person telling a narrative is seen to draw from social and cultural understandings to make sense of their experiences and construct their narratives, a researcher draws from such understandings, as well as their own personal background and experiences, to make sense of what they are being told (Bruner, 1990; Wertz et al., 2011). It can therefore be said that both the participant (in the telling), and the researcher (in the listening) look for how they can bring the different aspects of the story together so to understand it as a meaningful whole (Hyden, 1997).

The process of narrative analysis involves not only a consideration of how people have constructed their narratives, but also further construction by the researcher to give narrative form to what would usually otherwise be a disorganised collection of thoughts and events

(Polkinghorne, 1995). In this sense, Polkinghorne (1995) differentiated between “analysis of narratives”, where analysis is conducted with narratives that are already a coherent, complete story, and “narrative analysis”, in which a researcher constructs narratives from the elements of experience presented to them by participants. In the latter, which is relevant to most narratives arising from interview-based research, the researcher constructs a narrative from the stories and experiences a participant has shared by configuring the given elements (e.g., acts and events, characters) into a coherent plot, based on their interpretation of the meanings these hold for the participant (Polkinghorne, 1995). The final product, the formed narrative in which events, acts and other aspects of experience are organised in a coherent, temporal and meaningful way, is thus a construction of the researcher’s interpretation of how a person understands their experiences, as well as how they have been understood by the researcher.

Therefore, social constructionism informs the process of narrative analysis on every level, specifically through foregrounding the influence of the setting and audience on the narrative that is told, as well as the joint construction of narratives by teller and listener; through emphasising the importance of the social, cultural and historical context in considering the meaning of experience, and the need for these contextual factors to be at the forefront in order for people to understand each other; and through the way the researcher interprets a person’s experiences in context, in order to construct a coherent narrative through which they can interpret the meanings of those experiences.

3.2.6. Narrative and illness

Illness, it has been said, calls for stories (Frank, 2013). The onset of serious or chronic illness can cause a sense of life upheaval, of “biographical disruption” (Bury, 1982) or “narrative wreckage” (Frank, 2013, p. 53), that can only be reconciled by the re-establishment of a narrative thread. Without the continuing sense of a narrative trajectory, a person loses the sense of who and where they are, and a sense of direction about where they are going (Frank, 2013). Because narratives are fundamentally about how people make sense of their world, they provide

an ideal theoretical and methodological approach for understanding how people make sense of their illness experiences. Illness narratives are not merely about illness, but also about a life that has been altered by illness (Garro, 1994). In contrast to the purely biomedical perspective that is prominent in Western culture, illness does not occur in isolation from other life experiences and contexts, but within the complexity of a person's life, which in itself is located within a wider cultural framework (Kleinman, 1988). Like any character that is woven into a story, the illness itself and a person's perception of their illness both have the capacity to change with the person, with the onset of new circumstances, perspectives, and with the passing of time. The narrative arises from the intersection between what it means to have illness from a personal and cultural perspective, the experience of the physiological symptoms of that illness, and their impact on each other. From this dynamic exchange arises the lived experience of illness (Kleinman, 1988). Analysis of illness narratives can therefore provide great insight into the way people incorporate illness into their lives and make sense of it amidst all of these complexities.

Numerous events feature during the course of illness, with obvious examples being the development of symptoms, diagnosis and treatment. Narratives enable these often-medicalised events to belong to someone, and to let that person have a voice with which they can share their unique experiences (Hyden, 1997). They allow people to bring these events together, relate them to each other and, particularly in the case of chronic illness, to the experience of suffering over time. The way that people experience these events, their sense of agency and the outcomes they aspire to, differ from person to person, as each has their own personally- and culturally-specific lens through which they view the world. The order, emphasis and relationships that they portray in their narratives therefore provide insight into how illness is made meaningful for them within the culture they are part of.

Narratives can also go a step further than portraying the meaning of illness, and actually shape the illness experience. As it can be said that people live their lives according to narratives, these fundamentally determine the way in which they experience symptoms of illness and suffering

(Kleinman, 1988). For example, one person's narrative might include the perception that illness is a normal part of life, whereas for another person, illness might be seen as something abnormal and to be feared. Because of the divergence in their narratives, these two people will undoubtedly have very different experiences of illness. For this reason, personal narratives are often a focus of therapeutic work, in that the existing narratives that are holding people back in life are gradually replaced with narratives that will help them to move forward (e.g., Kropf & Tandy, 1998). To put it another way, the shifting of narrative structures can also alter the way that people feel about themselves, as well as their past, present and future (Garro, 1994). This is an important factor to consider when analysing narratives, as the narrative that is prominent in the present will affect a person's recollection of the past as well as their vision for the future.

In his seminal work, *The Wounded Storyteller*, Arthur Frank suggested that most illness narratives involve three specific narrative forms: *restitution*, *chaos* or *quest*, but also that other forms can and should be proposed (Frank, 2013). Furthermore, he put forth that while one form may be the prominent narrative at any one time, others will remain in the background, and they can continue to alternate through the telling of the story, "perpetually interrupting" each other (Frank, 2013, p. 76). By understanding the narrative forms that take the foreground and background when people talk about their illnesses, one can therefore gain insight into the nature of their illness experience.

3.2.7. Understanding narratives about living with psoriasis from a social constructionist perspective in this research

The preceding sections have given an overview of the assumptions of social constructionism, how these relate to narratives and narrative inquiry, and how narratives are the means by which people make sense of their lives and the world around them, and therefore how they also make sense of their illnesses. Each of these perspectives informs the current research throughout, as will now be discussed.

Firstly, the aim of this research is not to measure or categorise the ways in which psoriasis can

affect people's lives, nor is it to try and explain them, in a cause-and-effect manner as in taking an objectivist standpoint. Instead, this research will involve an exploration of the ways that people construct meaning from psoriasis and their psoriasis-related experiences, which then becomes their 'reality'. It is conducted with the assumption there is no 'true' experience of psoriasis to be found, but rather, that the way people experience psoriasis is inseparable from the way they understand it, and how people understand psoriasis is seen as arising from the meanings they attribute to it in the context of their lives overall, within their specific wider social and cultural setting. In this research, narratives are considered as the vehicles within which people organise, understand and make sense of their experiences. While the stories that people tell about their psoriasis are seen as being their own, based on their own unique experiences, the narratives underlying those stories, and therefore the ways in which people understand their psoriasis, are seen as all originating from wider, shared understandings. These shared understandings are considered in the analysis in relation to how they influence people's experience of psoriasis.

Secondly, as narrative inquiry from a social constructionist perspective involves not only a consideration of how people describe their experiences, but also takes into account the wider circumstances within which those narratives are told, people's circumstances and the context in which they share their experiences of psoriasis are viewed as important partners in the way that narratives are constructed. Thus, in the analysis, emphasis is given to participants' own backgrounds and histories in relation to how these impact the way they experience psoriasis. This also means that by taking part in interview-based research about their experiences with psoriasis, what a person says about those experiences is seen as being constructed specifically for (or with 'intentionality' towards) the particular audience in a particular setting (Mishler, 1986). That is, participants are seen as telling their story for a specific researcher (myself), who they can deduce has a particular set of obvious characteristics (e.g., female, interested in psoriasis, younger/older than themselves) that may or may not alter how they present themselves, and they are doing so knowing that they are taking part in a study about living with

psoriasis. Thus, the stories that people tell in the interviews for this study are viewed as particular constructions of experience, based on how a participant chooses (subconsciously or not) to present him or herself in that setting. In this process of construction, participants are seen to place emphasis on certain aspects of experience and not others, and thus to tell one particular story (or multiple stories) over others.

Furthermore, as social constructionism emphasises the importance of context in the meaning-making process, this means it is necessary for myself as the researcher to reflect on my role in the construction of participants' narratives. My involvement in the construction of meaning is seen as beginning from the moment a participant engaged with information about the study and responded to how the study was advertised and described. It is then seen to continue throughout each interaction with a participant before, during and after the interviews themselves, as each interaction influenced both my impression of the participant and *vice versa*, both of which contributed to how the narratives have been presented and understood. As the researcher, I also bring with me a unique perspective based on my own personal background, nested within a wider social and cultural framework. As the way that I understand and interpret the meanings of participants' narratives is inseparable from my own background, I consider the ways in which my own presuppositions and circumstances contribute to the narratives that I ultimately identify; I describe this process of *reflexivity* further in section 3.3.5.

Finally, not only are the stories people tell about their psoriasis seen as representing the way in which they construct meaning from their experiences, but my interpretation and analysis of narratives involves further construction based on how I understand what it means to live with psoriasis. That is, through my attempts to understand the meanings that a participant attributes to their experiences with psoriasis, I construct another level of meaning through my interpretations. Furthermore, in interviews, people do not often present their experiences clearly as fully formed narratives; that is, as coherent, temporally-ordered stories in which the linkages between elements of the story are clear, explicating the meanings the person attributes to them, and with a clear progression towards a goal. Therefore, in order to analyse the narratives that

people use to make sense of their psoriasis, I must first actually construct the narratives; a process of construction that is based on interpreting the meanings that people attribute to their experiences and how they fit together to form a cohesive narrative that fits with the contours of their stories. People's stories provide ambiguous representations of their experiences that could be interpreted in a number of ways (Riessman, 1993), therefore the meanings of narratives presented in this study should be seen as my interpretation of the meanings people attribute to their experiences with psoriasis, inseparable from my own background and circumstances. The process of narrative analysis that was employed in this study is described in detail in section 3.3.4.

3.3. Methods

3.3.1. Recruitment

It was estimated that between eight and twelve participants would allow a range of different experiences of psoriasis to be explored. Participants had to meet two criteria: to have had chronic plaque psoriasis for at least two years, and to have been officially diagnosed by a dermatologist. The reason for the first requirement was because this research relates to the effect of psoriasis on one's life over time, and those with recently diagnosed psoriasis would not have had adequate time living with the condition to portray this. The second requirement was based on the common occurrence of misdiagnosis in psoriasis that was observed in conducting the vitamin D trial (presented in chapters 5 and 6), whether due to self-diagnosis or to diagnosis by medical professionals inexperienced with psoriasis.

Five people were initially recruited *via* advertisements through the university's email network, which had been subsequently passed on through people's personal networks. The email advertisement for the study is included as Appendix 1. Interested individuals got in touch *via* email, and were then contacted by phone to explain the research to them and to give them the opportunity to ask questions. The underlying purpose of getting in touch by phone rather than reply email was to begin to build a sense of rapport with the participants, and to make sure they

felt comfortable about taking part. Following this phone call, participants were emailed an information sheet explaining the purpose of the research and the procedures involved in the interview process in more detail (Appendix 2). Each person who had inquired about taking part in the research was subsequently happy to take part. An appointment was made either over the phone or by email to meet for the interview, at a time and place that was convenient for them.

As I knew it was possible that people I came into contact with on an everyday basis might know someone with psoriasis, or even have it themselves, I also made efforts to talk about my research with others in the hope of finding additional participants. I recruited two participants this way; one contacted me after being given my details by a friend, and another gave me her contact details when she overheard me talking about my research to someone else. These people were contacted and appointments were made in the same manner described above. I had originally planned to limit recruitment to people in Wellington so I could meet with participants face-to-face, yet over the course of three months I had only found seven local people to take part. As I knew of three others in different parts of the country who were willing to participate, I decided to include them and to conduct their interviews over Skype. Two of these people were friends of friends, and the other had been part of the vitamin D trial and had expressed interest in being interviewed. Interviews were conducted with participants as they were recruited, meaning that by the time these last people were recruited, seven interviews had already been conducted and transcribed. Although identification of the narrative forms used by participants (as described below) was still a work in progress at this point, by the time I had transcribed these three further interviews, I could see many similarities between these experiences and those I had transcribed earlier. Taking this into account alongside the challenges in finding more participants, it was decided that these ten people would suitably comprise the group of participants for this research.

3.3.2. Participants

The participants were eight women and two men, six of whom were based in Wellington, New Zealand, and four who were from other New Zealand cities or towns. Participants were aged between 34 and 88 years old, and each had had psoriasis over a long period of time (between 14 and 80 years), with most having had it for at least half of their lives. While objective psoriasis severity was not a direct consideration in this research, at least four of the participants were eligible to receive systemic or biologic treatment, indicating more severe psoriasis; a fifth participant also described extensive hospital visits and treatment as a child, before such treatments were available. Four participants mentioned having been diagnosed with psoriatic arthritis, and for two of these, arthritis was a significant part of their psoriasis experience. Three others also mentioned symptoms of arthritis, but not a diagnosis, and not as a central part of their stories. Seven participants were in supportive relationships, and the two who had been widowed described having close family and friends. The majority of participants were working, with three either approaching retirement or retired. Researcher-assigned pseudonyms, demographic and psoriasis-related characteristics of participants, along with treatment history, are presented in **Table 4**.

3.3.3. Ethics

Before beginning this research, ethical approval was sought and obtained from the Massey University Human Ethics Committee under reference MUHECN 12/076 (Appendix 3). Through the ethics application process, I identified that giving the participants the opportunity to talk about their experiences, and perhaps to understand them more fully as a consequence, may be possible benefits of taking part in the research. I also acknowledged the potential for emotional discomfort when talking about painful periods or experiences in one's life, and the sense of vulnerability that might arise when sharing personal and private feelings and experiences with another person. In response to these potentials, I did my best to establish and maintain a good rapport with participants, and to help them to feel as comfortable as possible. I adhered to respectful and considerate interviewing practices in which participants were aware

they could stop and withdraw any information they were uncomfortable with. I made sure participants were fully aware of their right to not discuss any issues they did not want to, which I reiterated if I felt I was addressing a potentially sensitive topic for them, and reminded them I could turn off the recorder at any time. Therefore, I balanced my desire to hear as much detail as possible with ensuring that participants only shared what they felt comfortable to.

3.3.4. The interview process

Interviews were conducted from June to September 2015, and interview lengths ranged from thirty-five minutes to two hours and twenty minutes. Participants were interviewed at locations convenient to them: four participants were interviewed in a private room at Massey University's Psychology department, two participants were interviewed at their place of work, and one participant was interviewed in her home. The other three participants were interviewed over Skype due to being located in different parts of the country. In one case, the connection was not good, and after a short time it was decided best to continue the interview over speakerphone. Where applicable, participants were reimbursed with a voucher for travel costs. Before the university-based interviews, participants were offered tea, coffee or water before beginning to ensure they were comfortable, and for those in different settings, they were asked if they felt ready and were equipped with water, tea, etcetera before beginning the interview. The interviews were instigated with friendly chat to help participants feel at ease, then the aim of the research was restated, and participants were thanked for offering to take part. Important factors in the information sheet were then reiterated as a reminder for participants: that the interview would be recorded, but that they could request that the recorder be switched off at any time; that they did not need to talk about any topics they did not want to; that the interview would be directly transcribed by the researcher; and that information pertaining to their identities would be removed from transcripts and they would be identified with pseudonyms in any quoted material. Participants were also advised that they could withdraw from the research for up to a week after the interview, with no questions asked, if they changed their mind about taking part;

Table 4. Participant characteristics and treatment history

Pseudonym	Age bracket	Years since diagnosis	Psoriatic arthritis symptoms?	Current treatment type for psoriasis	Previous treatments for psoriasis ¹	Marital status	Work status
Cara	Mid 30s	~16	N	Topical	Topical / systemic steroid	Married	Employed
Carrie	Early 40s	~14	Y	Biologic	Topical / systemic	De facto	Employed
David	Late 30s	~14	N	Topical	Topical / systemic steroid	Married	Employed
Jane	Late 50s	~50	Y	Topical	Topical	De facto	Employed / student
Logan	Early 50s	~40	Y	Systemic	Topical / PUVA	Single	Employed
Penny	Late 40s	~30	Y	Systemic	Topical / PUVA	Widowed	Employed
Sally	Mid 60s	~30	N	Topical	Topical	Married	Semi-retired
Sarah	Late 80s	~80	Y	Topical	Topical	Widowed	Retired
Tessa	Late 50s	~30	Y	Topical	Topical / systemic	Married	Self-employed
Victoria	Mid 60s	~40	Y	Topical*	Topical	Married	Semi-retired

PUVA, psoralen + ultraviolet-A

¹‘Systemic’ refers to methotrexate, ciclosporin or acitretin, while ‘systemic steroid’ refers to e.g., prednisone.

*Also on systemic for psoriatic arthritis

this timeframe was stipulated because only a limited amount of analysis would be done by this point, and to ensure there would still be time to recruit further participants if necessary. They were then asked if they had any questions before the interview began. Following any questions, participants signed a consent form formally agreeing to take part (Appendix 4). For one participant interviewed over Skype, the consent form was emailed, signed and scanned prior to the interview. In the case of the other two Skype interviews, which were conducted with minimal notice and without the availability of scanning facilities, verbal consent was obtained on audio recording prior to the interview, and these were followed up with posted hardcopies of the consent form. The interviews were digitally recorded on iPod, and the participants were asked permission before the recorder was turned on. All participants were happy to be recorded, and at no point during the interview did they ask that the recording process be stopped.

The interviews were semi-structured, in that topics, questions and prompts had been prepared in advance to ensure all the relevant areas were covered (Appendix 5) but they were as participant-led as possible in order to gain insight into which aspects of their experience participants felt were most important to share. Adopting this approach meant that the interviews were conversational in nature, and at the same time the participants were enabled to do most of the talking. The interviews were opened with some variation on the question: “Can you please tell me about when you first realised you had psoriasis?” As the researcher, I followed participants’ leads as to what was important and significant for them, and in this sense, was always open to the possibility of stories developing in unexpected places, around topics that might not have immediately appeared important. When the participant spent time discussing something that seemed to depart from the topic, it was viewed as an opportunity to learn more about how the participant constructed their identity and their world, and thus as enriching my overall understanding of their narrative. Therefore, I did not restrictively try to keep them ‘on track’. That said, in some instances this kind of dialogue became drawn out, and then I did my best to gently bring it back to their experiences with psoriasis. If the meaning of something a

participant said was unclear, further questions were used to probe for more meaning, and to prompt them to describe what certain events or situations meant for them. Often, participants naturally covered most of the areas that I had wished to cover in the interview, and therefore many of the questions were not required. For any areas that the participant did not naturally address, relevant questions were asked when the time was appropriate, that is, if they logically led on from related topics, or when the participant did not seem to have more to say.

Notes were made during the interview, in order to capture any references that might not have been clear on the audio (such as referring to a certain body part as 'here'), and to note down any points that I wanted to come back to or questions that arose from what the participants said. Notes were also made immediately after the interview, and in these I recorded my impressions of how the participant had come across within our interaction (e.g., were they reserved, confident...?) and of the way I felt they had presented themselves within their stories (e.g., as determined, 'a fighter', 'on a mission', passive...). I also noted down my first impressions of what their story was about (e.g., were they actively trying to overcome their psoriasis or had they learned to live with it...?) In this sense, analysis of the narratives began during the interview process, and continued throughout the transcription and closer analysis as described in sections 3.3.5. and 3.3.6.. Also, the interview prompts continued to be developed as I conducted more interviews, and new questions and better ways of saying things arose.

The interviews were concluded when all the relevant areas had been covered and I felt I had a good understanding of a participant's story, and when the dialogue between us had naturally drawn to a close. To finish, I thanked them for sharing their experiences, explained that I would be embarking on the process of analysis and they would receive a copy of the findings when they were complete. I also asked if they would be happy for me to call them to clarify anything that might come up during the analysis, and all were happy for me to do so.

3.3.5. Transcription

Interviews were all transcribed by myself, in most cases within two weeks of the interview taking place. Participants were given pseudonyms to ensure their privacy, and these were used throughout the transcript and for all other documentation, including naming audio files saved to computer. Other than the alteration or exclusion of people's names and other features that could identify the participants, transcription was verbatim. In line with a social constructionist perspective, I viewed the dialogue that took place as being co-constructed by the participant and myself, and therefore also included my own questions, responses and other notable utterances along with the participants' in the transcripts. I paid attention to short and long pauses, as well as utterances such as "um", so that the way I understood what participants said and where they had had moments of consideration, respectively, could feature in the transcript. I also noted where they cut off the end of a sentence, as I felt this was often meaningful in itself – sometimes suggesting a reconsideration of ideas, sometimes a moment of confusion in dialogue between the two of us. I noted when either the participant, or myself, or both of us laughed, as this indicated the tone of what was said. Once the transcript had been typed out, I listened to the audio recording once more while checking the transcript for any errors. Because it was important to me to capture the particular way participants spontaneously constructed their stories in our dialogue, they were not provided with copies of their transcript for checking.

3.3.6. Narrative analysis

There is no one prescribed way in which to conduct narrative analysis, but various approaches have in common a focus on how people interpret things (Bruner, 1990), and from there, involve an interpretation of their interpretations (Riessman, 1993). The interpretation of narrative is based on the theoretical assumption that people make sense of their lives by framing them within narratives (Bruner, 1990), and therefore, studying the narratives people use to describe their experiences offers insight into the meanings that they ascribe to those experiences. Arriving at the final method of analysis in the current research was an organic process that took place over several months. I will begin by describing how I first approached the individual

narratives, how the process of analysis changed over time, and then how I was able to develop the overall narrative structures that are presented in the findings.

As stated above, the analysis began during the interviews and transcription process as I formed my thoughts and impressions around people's experiences, and these initial thoughts informed the rest of the analysis as it progressed. I then worked through the interview transcripts one by one; once I had checked a transcript against its recording, I printed it out and read it a number of times to immerse myself in what the participant was saying. I also made notes of my initial thoughts in relation to parts of the transcripts that stood out as being important to a person's experience. As I was unsure how to proceed with the analysis from that point, I began with the suggestions put forth by Murray and Sools (2014), which involved consideration of how participants used Burke's five narrative elements (i.e., agent/character, acts/events, means/helpers, setting/scene, goal/purpose) (Burke, 1969), along with a breach/trouble, in describing their experiences, and construction of a story based on these elements. In line with Polkinghorne's (1995) suggestion, I placed emphasis on understanding the overall goals that participants seemed to be focused on in their stories. I interpreted the goals of the individual storylines by asking myself, where does each storyline end up? Was it where the participant wanted to end up? After first identifying the goal of the story, I then considered each of Burke's narrative elements in relation to whether they helped the participant to progress towards their goal, or hindered their attempts in this regard, and why. For example, if a person's goal was to find a cure for his or her psoriasis, I then considered the acts and events that contributed both to the development of this as a goal, and also what the person did to try and realise their goal. In doing this, I also noted that some participants had a 'turning point', in which something happened in the participant's life and it caused them to shift their goal. Once I had described the different narrative elements of each participant's story, I then gave the storyline a name based on the goal and constructed a narrative for each participant. This was done by chronologically ordering and linking the acts and events, along with other elements of the narratives, in such a way that both connections that participants had explicitly stated in their

interviews, as well as my interpretation of the connections in their experience, gave an overall sense of meaning to the story.

As I continued working in this way, and due to the number of times I had listened to the audio recordings and read through each transcript, I found I was able to more easily identify the goals of other participants' stories and the different aspects that contributed to or hindered their achievement. I therefore began to first name the overall storyline for each person, and then to write that storyline based around the acts and events that took place over time, making notes as to the important features in the narrative (e.g., other important characters, means/helpers towards the goal, turning point), and I then also wrote an abridged version of the storyline to home in on its most important aspects. The abridged storyline for each participant, along with their psoriasis history and a brief personal background are included as Appendix 6. As I progressed with the analysis of individual narratives, similarities and differences between them began to become evident. The most obvious difference was in the goal they progressed towards: I could see some people were focused on overcoming their psoriasis, while others were more accepting towards living with it. I described these early narrative forms in detail and used them as 'working' forms that I developed and changed as I continued to analyse participants' stories. For each new participant's story, I considered whether it fit with one of the forms, and adapted my understanding of the narrative forms accordingly.

The most significant changes occurred following my observation that participants were describing similar experiences regarding the time following their diagnosis, and that they progressed to one of the two other (continually further refined) narratives following a turning point of some kind. This gave me a sense of how people's experiences might follow a more complex narrative trajectory over time than I had initially considered. As I further refined the major aspects of my working narratives, I realised that the way participants described their experience of psoriasis following diagnosis, as well as much of what I had initially thought to be a separate narrative (but turned out not to be), aligned with the restitution narrative, which Frank (2013) describes as a narrative in which a return to health is sought. Furthermore, when I

considered the parts of the experience I had described as turning points, I was aware that for several participants, their turning points involved significant suffering that I had not yet captured in the narratives I had developed, and that this suffering aligned with the experience of a chaos narrative, as also described by Frank (2013). To ensure I was not being 'led' by these already-established narrative forms, I summarised their characteristics and compared them with the storylines I had written for each participant, as well as going back to their transcripts and identifying the characteristics of the narratives amongst participants' words. I could also see occasional hints of the narrative form Frank describes as a quest narrative. The characteristics of these narrative forms are described in more detail below, and are summarised in **Table 5**. Yet, none of Frank's narrative forms related to the other narrative I had identified in my analysis and which was used by almost all participants at some point, in which acceptance of psoriasis was the focus. I developed a description of the characteristics of this narrative by considering the following questions in relation to participants' experiences: How are psoriasis and its treatments perceived? Who or what has agency? What kind of actions and events does this narrative entail? How does this narrative arise? And, what are its limitations? Again, the transcripts of participants whose storylines involved this narrative were revisited in detail to answer these questions and to ensure the use of this narrative was evident in their own words. This process led to the identification of a narrative form that I felt was best described by the name *resignation* (described in more detail below).

The final step was to consider how participants shifted between different narrative forms over time in relation to their experience with psoriasis. At this point, I constructed a narrative timeline for each participant, which began at the point when their psoriasis first developed, progressed through the post-diagnosis period, different life events and fluctuations in psoriasis, and ended in the present. For each of these stages in a participant's timeline, I noted which narrative form they had used when describing that time, and any known influences on why it was experienced that way. In this way, I determined how participants shifted between narrative forms in relation to different stages of their experience with psoriasis, and factors that might

have contributed to these shifts. To support the identification of each participant's narrative trajectory, it was also compared with the overall storyline I had written for him or her at in the earlier stages of analysis. The different narrative trajectories followed by participants in this study are presented diagrammatically in **Figure 3** on p. 107.

3.3.7. Reflexivity

As has been discussed, the process of narrative analysis is not a matter of the researcher 'uncovering' a person's story and providing an exact representation of reality (Polkinghorne, 1995). While it is important to try and stay true to the participant's intent, this takes us back to the questions of where meaning is found, and indeed, whether there is a 'true reality' at all. The social constructionist approach of this research means that narratives are seen as being jointly constructed by both the researcher and the participant; the participant tells the story, but he or she is telling it *to* someone (i.e., the researcher), and thus the story that is told is inevitably influenced because of the mere presence of the researcher. Furthermore, the researcher is an active participant in the interview process, and the dynamic interactions that occur between the participant and the researcher jointly contribute to how the interview unfolds (Finlay, 2002). It is also crucial to note that the narratives developed from participants' interviews, and the discussion of the narrative forms in the following Findings section (3.4), are my *interpretations* of participants' stories and their meanings. Because of the crucial and fundamental role that I, as the researcher, have played in the construction of narratives and their meanings, it is therefore vital that I am cognizant of the ways in which I have contributed to the construction of the narrative, and thus, to shaping these findings (Finlay, 2002). This act of having a thoughtful, conscious self-awareness throughout the research process is described as reflexivity (Finlay, 2002), a process that has been more thoroughly defined as a "consideration of the assumptions, positionings and relationships surrounding the researcher and its interpretation and representation" (Chamberlain, 2015b, p. 170). By including such considerations in the presentation of research, reflexivity therefore allows those reading the research to better understand the meaning of the findings.

A first point of importance when considering my position in relation to that of participants is that I do not have psoriasis, nor another visually comparable condition. I am therefore aware that this probably meant there was more distance between each participant and I than if I had also had psoriasis. At the same time, all participants were aware that I had spent a number of years researching psoriasis, and that I had interest and knowledge in this area, and so they may have considered me 'on their side' and thus, trustworthy. The relationship between myself and many of the participants in the interviews could therefore be described as one in which they took on the task of explaining to me what it was like to have psoriasis, assuming little personal insight of the experience on my part, yet knowing that I had some level of understanding of and interest in the disease. On the other hand, unbeknownst to participants, I have previously suffered from skin conditions that have been physically challenging and caused me to feel self-conscious, and I see my experiences with these conditions as having given me greater empathy towards people with psoriasis. I believe this empathy was a crucial part of the way I approached the interviews, and this is supported by how several participants chose to share very personal experiences that they did not find easy to talk about.

As I had already conducted the trial into vitamin D and psoriasis (as described in chapters 5 and 6), I was also very conscious of how my experiences with participants in that trial affected the way I approached this qualitative study. In fact, those experiences had inspired this narrative research, as my interactions with participants involved in the trial had shown me that people with psoriasis had stories that needed to be told and understood. Therefore, by the time I entered into interviews with participants, I had already had numerous brief conversations with people about the impact of psoriasis on their lives, and I had read a range of previous research studies pertaining to this area. However, in light of the overwhelmingly negative nature of the literature on living with psoriasis, what the trial participants had also taught me was that people are affected by psoriasis in myriad ways; I knew some of them felt debilitated by the condition of their skin, while for others, it was of little concern, and for still others, it had previously caused suffering that had then abated over time. Therefore, I approached the interviews with an

effort to have no preconceptions about how a person might experience psoriasis, or about what I might learn from them, and had the view that every experience was valid in its own right and had something to offer. My goal was to provide the most open and warm atmosphere possible, so participants would feel comfortable to share their experiences. I specifically reflected on this after one particular interview, in which the participant, whose psoriasis was limited to her scalp and obscured by her hair, suggested that I might not be interested in her experience as her psoriasis did not bother her too much, especially compared to her friend and “perhaps I would like to talk to him instead?” Although I had thought I was being open to any and all types of experience, I realised that the way I asked questions about how psoriasis had been limiting in their lives could be interpreted as me putting more value on experiences in which people have suffered to a greater degree. From that point, I was even more conscious of trying to remain open and as neutral as possible as I met with participants and heard their stories.

Something else that working with people in the vitamin D trial gave me was an experience-based understanding of the sensitivities many people have in relation to talking about their psoriasis. One participant even highlighted this in her interview, commenting on how odd it felt to be talking about her psoriasis not only at length, but also at all. This understanding meant that I was even more aware of the gentleness and sensitivity of approach that was needed in my interactions with participants, and I was careful to try and provide a comfortable (rather than awkward) space in which participants could share. I feel that this approach was successful and added to the quality of the interviews. The personal details people shared added to the richness of the interviews and the understanding of how and why a particular narrative might have arisen, and thus perhaps why a person’s experience with psoriasis was as it was.

During the process of narrative analysis, through which I interpreted how participants had experienced their psoriasis and constructed narratives describing that experience, I also considered how many of my underlying assumptions and beliefs contributed to the findings. One of the most prominent in this regard was where I considered the sense of begrudging associated with the acceptance of psoriasis, the lack of dominant quest narratives, and which of

the narrative forms followed after chaos narratives, as will be described in detail in the following section. My own philosophy of life is one in which I try to see difficulties as obstacles to be overcome, and struggles as a prerequisite for personal growth. Therefore, I was aware of my focus on whether any of the participants viewed their experience of psoriasis in this way, and this focus is reflected in the findings. I was also always aware that the data I was working with could be interpreted in multiple ways, and that my personal background and assumptions would influence the interpretations I made. I was even aware of this through my own process of analysis, as the earlier narrative forms I had constructed had points of differentiation between them that were no longer a focus in the final narratives I presented, as I had shifted my perspective on how psoriasis was experienced. Once I had developed the narratives I have ultimately presented in this thesis, I found it more difficult to consider what other interpretations of the narrative might specifically be, however, I was always conscious that these were only one of multiple representations that these findings could take.

Therefore, as this thesis moves into a presentation of the findings of a narrative analysis of living with psoriasis, what follows should be understood as not the *only* narratives that people use to describe living with psoriasis. Instead, they are narratives that *have* been used to describe the experience of psoriasis, and furthermore, are based on my interpretation of the experiences participants described in interaction with me as the researcher. As a preface to the presentation of narratives identified in this study, my interpretation of Frank's three narrative forms described in *The Wounded Storyteller* (Frank, 2013), as well as a description of the resignation narrative, will now be given.

The restitution narrative

The restitution narrative follows the basic premise that “yesterday I was well, today I am sick but tomorrow I will be healthy again” (Frank, 2013, p. 77). Illness is therefore seen as a temporary disruption to normal life, and the protagonist is focused on overcoming their illness, and returning to their prior state of better health. This reflects the predominant cultural view that health, and not illness, is the ‘normal’ state of being, and that an ill person should, and even

has the right to, have their health restored. For this reason, the restitution is the most culturally desirable narrative related to illness, and people may tell this narrative because they think it is what others expect to hear.

The restitution narrative is anchored in the biomedical view of illness, where an illness develops, is diagnosed, treated and then cured. The ill body is seen as being akin to a machine that has broken down, and can therefore be fixed with the appropriate treatment. The storyline is focused on attempts to restore health: tests and their outcomes, treatments and their efficacies and doctors and their competence. In fact, it is the treatments and the doctors that are the active players in this narrative, not the person telling the story. The success of the narrative depends solely on the efficacy of the treatment or the doctor; the protagonist, on the other hand, is without agency, as he or she cannot determine the outcome.

Restitution is probably the most common type of illness narrative for acute illnesses, reflecting the natural desire of most sick people to regain their health. In this sense, therefore, it is a hopeful narrative, but the hope is pinned solely on the restoration of health, without room for alternative outcomes. This presents challenges for the use of this narrative form in cases of chronic illness. It is also the most culturally desirable narrative relating to illness, as 'health' is considered the default state that people should aspire to return to, and a person who is ill for an extended period of time, or who expresses uncertainty about returning to health or about the future may prompt a sense of discomfort in others.

The chaos narrative

While restitution means to hold onto the hope of becoming well again, chaos is what happens when the gap between reality and the ideal of health becomes so wide it seems insurmountable, and the reality feels too painful to sustain. Chaos narratives are entirely suspended in the present moment, in the sense that the current suffering feels inescapable, and the future cannot be contemplated. Life as normal essentially goes on hold as the illness takes over the foreground. Illness is neither accepted nor made sense of, and a sense of hopelessness pervades.

The illness is perceived to be more powerful than the person, and it can impinge on identity and even overtake it.

Frank actually describes chaos as an “anti-narrative” (Frank, 2013, p. 98), as the experience of chaos is devoid of the coherence, contingency and temporality that are definitive parts of narrative structure. This is because the person’s own voice, necessary for narrative, has become lost as their suffering has become too great, for chaos represents the experience of being “sucked into the undertow of illness and the disasters that attend it” (Frank, 2013, p. 115). Chaos can only be understood as a narrative when the person is no longer in it, and has regained the ability to reflect on their experiences.

The quest narrative

In the quest narrative, the protagonist seeks to meet suffering head on, and to use it to create something of value for both themselves and for others. While it may never be clear what that something of value is, the defining aspect of a quest narrative in illness stories is the belief that something is to be gained from the experience. The canonical quest story is that of the Bodhisattva, a being aspiring to the enlightened state of the Buddha, who understands that the purpose of suffering is to undergo personal transformation that can ultimately serve as encouragement to others who are also suffering. This personal transformation occurs at a fundamental level, and is evidenced by changes in the person’s behaviour. Illness is not necessarily seen as a positive experience, but the value of the illness journey is acknowledged, usually in retrospect. The quest narrative is the only one of Frank’s narrative forms in which the teller has complete agency; they own their illness experience rather than being at its mercy, and maintain a strong sense of identity and the power of choice.

The resignation narrative

In the resignation narrative, illness is accepted as permanent, and the focus is on trying to get on with life. Yet, the acceptance is of a reluctant, begrudging nature, due to the ongoing challenges that accompany living with and trying to manage the illness. Treatment regimes may still be

maintained, but only with an expectation of gaining temporary relief. As this narrative depends on being able to accept illness, its relative severity and stability must be within a person's 'bounds of acceptance'; that is, the illness must remain at a level that he or she feels personally able to live with. So long as the illness stays at this level, a person does not feel controlled by it, even if they are aware that it could worsen. On the other hand, if the illness progresses beyond a person's 'bounds of acceptance', a person is no longer able to accept it, and it becomes impossible to sustain this narrative form.

The key characteristics of the restitution, resignation, chaos and quest narratives are summarised in Table 5. With the general characteristics of these narrative forms having now been set out, this thesis turns to a presentation and discussion of the specific narratives that were identified in people's experiences of living with psoriasis.

Table 5. Characteristics of narrative forms identified in experiences of psoriasis¹

Restitution	Resignation	Chaos	Quest
<ul style="list-style-type: none"> • Focus on return to health • Illness is seen as fixable and therefore temporary • Lack of agency for teller; power lies with something external (e.g., treatment, diet, physician) • Driven by sense of illness as intolerable for self and possibly others • Can help sustain a sense of hope • Sacrifices (e.g., time, money, side effects of treatment) seen as necessary and justifiable for the sake of wellness • When complete, is the culturally-preferred narrative of illness • Can only be sustained so long as teller believes there are options available to pursue 	<ul style="list-style-type: none"> • Focus on getting on with life in spite of illness • Illness is seen as unfixable and therefore permanent, so is begrudgingly accepted • Capacity of treatment is seen as limited to managing illness at best rather than as cure • Future is viewed as an unchanging continuation of the present: living with and managing illness • Agency appears to reside with the teller, who cannot control illness but does not let illness control him or her, but; • Can only be sustained so long as illness remains within 'bounds of acceptance' 	<ul style="list-style-type: none"> • Without focus; living this narrative is incoherent and 'chaotic' • Can only be told as a story retrospectively, as reflection is impossible from within it • Teller has no agency, and neither do treatments; all power lies with the illness • Self is dissociated from body, but illness overpowers sense of personal identity • A sense of perpetual hopelessness and suffering prevails • Can be prompted by dramatic worsening of severity and stability of illness • Must be accepted in order to emerge from it, but can never be vanquished 	<ul style="list-style-type: none"> • Focus on facing suffering head on, and using it to create value • Illness is accepted, experienced in its entirety and integrated as a critical aspect of the teller's personal journey • Involves fundamental changes to the teller's character, evidenced through their behaviour • Purpose of the journey is understood retrospectively, and realised to be not just for the benefit of self but also for others • Teller has complete agency, which persists throughout fluctuations in illness

¹Descriptions of restitution, chaos and quest are my interpretations of the illness narratives described in Arthur Frank's *The Wounded Storyteller* (2013). The resignation narrative is an additional narrative type identified in the psoriasis stories.

4. Study One: Findings and Discussion

This chapter describes the first set of original findings presented in this thesis, which relate to the aim of gaining a greater understanding of the experience of living with psoriasis. It begins with a presentation of the findings that arose from this research, and these are followed by a discussion of the meaning of the findings within the context of the wider literature.

4.1. Findings

Each of the restitution, chaos and quest narrative forms was identified in participants' narratives about psoriasis, although quest was not a dominant narrative form and was the least common. I also introduce a fourth narrative type that was evident in most of the narratives, which I term the resignation narrative. In this narrative, illness and its associated symptoms and burden of treatment are begrudgingly accepted, so that the person may get on with their life. The resignation narrative differs from the quest narrative in that no good is seen to come from the illness, but in contrast with the chaos narrative, the person still has agency, and they choose not to put their illness at the centre of their life, or to let it dominate them.

The findings of this study demonstrate how the experience of psoriasis, as evidenced by the use of different dominant narrative forms, can differ over time with the fluctuating course of psoriasis and with progression through different life stages. The sections that follow will elucidate the major narrative forms that participants used to describe their experience of living with psoriasis, the different trajectories that were followed by each participant (Figure 3), and what these narratives can tell us about the experience of living with psoriasis.

4.1.1. The restitution narrative

In the restitution narrative, the focus is on overcoming illness in order to return to the healthy state of before. Because people who are sick generally want to be well again, and the people around them also desire their recovery, the restitution narrative is the culturally preferred

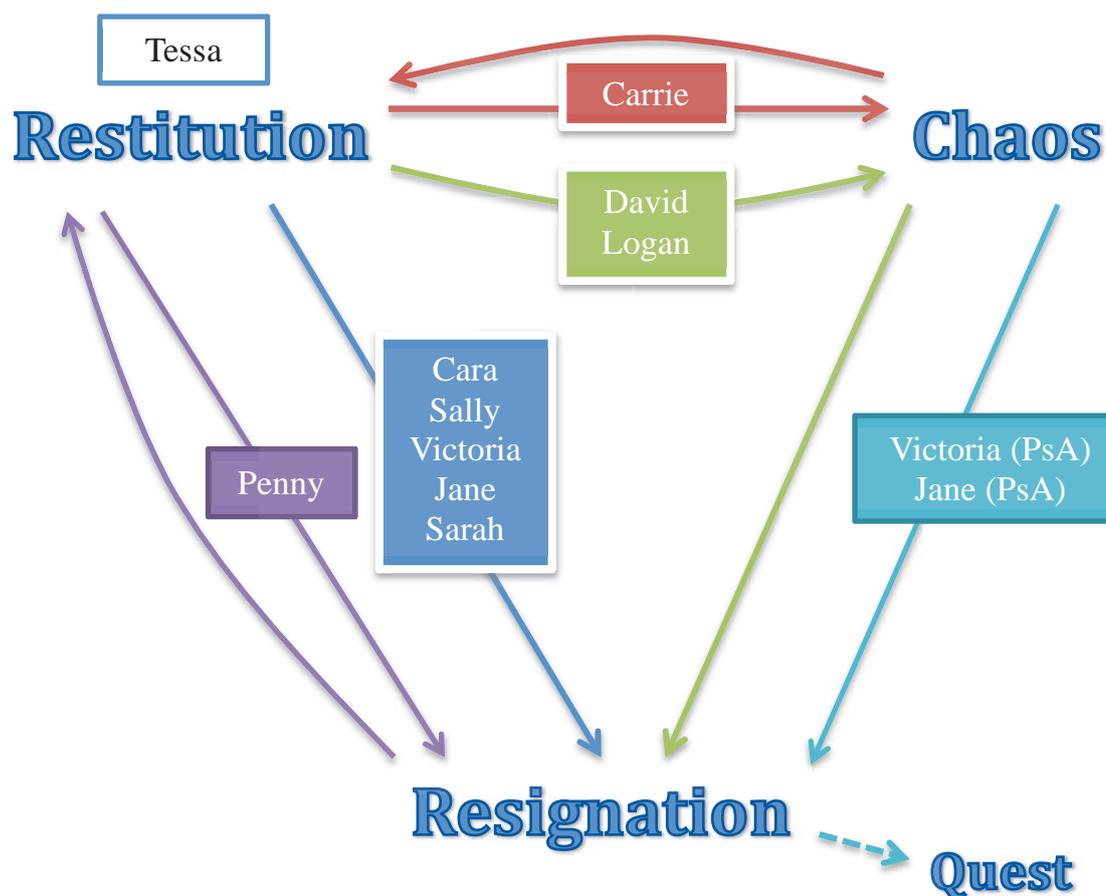


Figure 3. Different narrative trajectories in participants' experiences of living with psoriasis

PsA, psoriatic arthritis

Lines of the same colour are part of the same overall trajectory for that participant. The dashed line leading to quest illustrates that this narrative was only just in the process of emerging.

narrative around illness (Frank, 2013). This narrative was evident from the point when participants identified their symptoms as being out of the ordinary and sought medical advice. For most, psoriasis began with the development of one or more small itchy or red patch(es), which gradually worsened and became flaky and perhaps painful. This prompted a visit to a doctor and/or dermatologist, who identified it as psoriasis and prescribed various topical treatments. Most were told that as psoriasis had no cure, the aim was to manage it as best they could. Despite this, the restitution narrative was maintained: psoriasis was viewed as a temporary affliction, and participants held out hope that their psoriasis would be cured, or at least that their skin would be completely cleared.

You have this idea that things can be cured, everything can be cured, especially if you haven't always suffered from it, you think oh well, this is something that's temporary, so it'll, it'll get fixed. (Sally)

I was just trying to ignore it, yeah, as well, you know, hoping it would just, disappear, that, everyone was wrong, and that it will just, it'll just spontaneously go away. (Carrie)

The lack of known cure for psoriasis, coupled with its difficult, often impossible management meant that the restitution narrative in psoriasis stories remained stalled on a hope for clearance, as this was rarely achieved. Even when skin did improve, it was only temporary and usually dependent on treatments, and psoriasis was seen as having the potential to return at any time. In one sense though, the focus on treatments and becoming well again functioned positively as a source of hope, which was difficult to find elsewhere in relation to psoriasis. Doctors presented bleak outlooks of psoriasis, and other sources such as support groups or the internet painted a depressing picture of its permanency.

I was told it was a cross to bear actually, I had a couple of doctors say things like that and sometimes it's not that helpful. (Victoria)

The need for hope and the difficulty in being told that there was none was captured by Carrie, who summoned up her own sense of hope that she could overcome her psoriasis despite a lack of support and optimism from her doctor.

I don't think anyone should ever say there's no cure, what they should say is that I have not yet found something that I can help you, with.... When I first heard that from...my dermatologist...that was crushing...he was like, oh you know there's no cure ay, and I...could have slapped him, seriously, because I didn't wanna hear that, you know, I needed hope...and I think, when anyone's going through any type of challenges... if the

people that you turn to for help, have no hope for you, it's very difficult to have hope for yourself. (Carrie)

The restitution narrative also fostered a sense of agency in those with psoriasis; they felt that they were actually 'doing something about it'. Yet the irony of the restitution narrative is that the person in fact has no agency at all, as the success of this narrative depends entirely on the efficacy of the treatment/doctor. In the early years with psoriasis, however, just taking action towards restitution, and holding out hope that something would help, felt empowering in itself. To this end, storylines set in the years following diagnosis were based around trying treatment after treatment in the hope that something would cure psoriasis, or at least completely clear it. Most participants had tried an extensive range of treatments, and their associated inconvenience, side effects and risks, of which there were many, were seen as worth the effort if they were going to improve psoriasis.

I think at the start...I went all out to try and get rid of it, so I had hope.... (Sally)

I tried everything I could, you know, tried different treatments that might help better, you know... (Victoria)

As time went on, the motivation behind these efforts was also drawn from the growing awareness of the negative aspects of living with psoriasis. The idea of living with psoriasis for the rest of one's life felt intolerable, and many felt a sense of desperation to get rid of it so their lives could return to normal. Thus, the focus became less on the restoration of skin *per se*, and more on finding freedom from the difficult consequences of living with psoriasis.

Mm, try and manage it, yeah, I mean that's what they talk about, managing it, and it's like I don't want to manage it, I want to get rid of it [laughs]. I don't want to have to think about it every waking moment, you know...I just keep thinking, is there a cure for this damn thing... (Tessa)

The psychosocial consequences of psoriasis, such as immense feelings of self-consciousness, which became more established over time, continued to drive the efforts to achieve clear skin. The visibility of plaques and the constant shedding of scales caused significant embarrassment, to the point where participants frequently avoided normal social activities. When they did get involved, feelings of anxiousness and shame were prevalent, especially when the person worried that others had seen affected skin and/or scales. Restitution narratives persisted because the thought of having relatively clear skin was seen as the only way to feel better about oneself, and to experience life as 'normal'. Even when participants acknowledged that the power for overcoming this social discomfort resided within themselves, being able to do this seemed more impossible than finding a treatment to clear their psoriasis. Therefore, it was easier for them to place hope in something external.

Having psoriasis, I walk round in the world, and I think one of my biggest wishes, is that people didn't care, and that I didn't care as much, as I did, and do.... Sometimes it's easier to um, rather than do personal growth or personal development stuff, to just reach for a drug and, be done with it. (Carrie)

Being able to successfully treat or overcome psoriasis was also seen as part of avoiding stigma and rejection from others. Penny provided a detailed description of her treatment regime, and then said:

No one wants dry scaly things on there, 'cause people don't know what they are. It's not like there's something, zits that are coming up, um, you know what I mean, it's different, 'cause they go oh, what's that rash? I go, oh it's psoriasis and they go oh really you know, as though you're contagious. And I think people look at it and they think ergh. (Penny)

The long timespan over which the restitution narrative persisted without resolution of psoriasis illustrates the difficulty in finding a treatment regime that not only improves psoriasis, but does so to a degree that a person is happy with and can accept any associated side effects. In

participants' descriptions of the various treatment regimes they had tried, there was a significant focus on their negative aspects. Topical treatments presented challenges related to messiness, unsightliness and smell, the logistics of application, and the sense of money wasted. There was also concern about the long-term safety of topical steroids and systemic treatments. Initially, these drawbacks to treatments functioned in the restitution narrative as motivation to keep searching for more acceptable, effective alternatives. Over the longer-term, however, the lack of efficacy and the drawbacks of treatments caused some participants to start losing hope and begin to move away from this narrative form. For most participants, the balance of the treatment effort against the hope for significant results eventually tipped too far, and investing a lot of time, energy and money into treatments no longer seemed worth it.

They're saying it's going to do this magical thing that it's not gonna do, 'cause unless you can get rid of it, it's not worth it [laughs] and we know that it's not gonna get rid of it 'cause nothing has yet. (Cara)

As a result, the inability of treatments to cure psoriasis, or in some cases even control it, was reluctantly accepted, and this marked a shift away from restitution as the dominant narrative.

4.1.2. The resignation narrative

In the resignation narrative, a person begrudgingly accepts illness, along with any limitations of treatments and the need for ongoing management, in order to be able to focus on living his or her life. Overall, the illness is still viewed in a negative light due to the ongoing challenges it presents. Furthermore, this narrative can only be sustained so long as the severity of illness remains at a certain level; beyond that, acceptance becomes no longer possible and a different narrative must emerge.

For most participants, the shift from a dominant restitution narrative to one of resignation occurred when they had become tired of making significant, yet fruitless efforts to achieve full clearance of psoriasis, and had realised that there was nothing to be gained by continuing down

this path. All personally acceptable options for treatment had been exhausted, and holding onto hope in a major way had begun to feel like a hindrance. Therefore, participants let go of the hope for clearance or a cure, reluctantly accepted that their skin may never be clear, and looked for ways to cope with their psoriasis in order to get on with their lives. Six participants shifted from restitution to resignation, and for five of these, this was the full trajectory of their psoriasis story at the time of the interview.

You get to a stage where nothing seems to work long-term, and so, I just give up. [laughs] [Researcher: Right] And just put up with it, you know? My doctors have always told me, you can't make it go away, all you can do is manage it, and that's what I've, you know, I've realised I've just got to manage it the best way I can.... (Sally)

I didn't really sort of realise that it was only an ambulance at the bottom of a cliff kind of thing, that there is no, way to get rid of it, so I think back then I was a little more hopeful that it might actually fix it, um, but as time's gone on, I'm, I just, when it's just the next thing, you see the ads on TV...and there's this magical new shampoo, and you just go well, there was a magical new shampoo three years ago and that didn't work, so, you know, I just don't believe anymore [laughs] (Cara).

It's been so long, you know it's been 16 years, um you just kind of give up [laughs], you know, you try all the creams and the magical shampoos that they say are gonna help, and they don't, so you just sorta go ok, well this is it, it could be worse, this is my lot, it could be worse [laughs]. (Cara)

On the other hand, for one participant, moving from restitution to resignation occurred once she had found a treatment that effectively cleared her skin after a flare up. While she only took this systemic treatment intermittently in response to a major flare-up, knowing that she had access to something that could manage her psoriasis allowed her to begrudgingly accept a life with psoriasis and its contingencies. Although the reliance on treatment and focus on clear skin is reminiscent of the restitution narrative, this participant's story was not centred on a return to

health as in restitution. Instead, it told of her efforts to try and get on with life despite the constant threat or actual presence of psoriasis, which is at the core of the resignation narrative. Furthermore, the sense of begrudging was clear, as prominent in her stories were the challenges that arose from these flare-ups, such as feelings and consequences of her immense self-consciousness, fear of the risks involved in using systemic immunosuppressants, and the difficulty in applying topical treatments while waiting for the systemic treatment to take effect.

For others, the shift to a resignation narrative followed chaos. This transition involved the shift from hopelessness and powerlessness, to acceptance and a sense of being able to get on with life. It was spurred by the decision to reclaim a sense of power over their lives after having reached some version of 'rock bottom' in chaos, and the actions they took to do so. One participant, David, described this as a process of "unwinding" all that had led to his breakdown. Another, Logan, developed strategies to help him view psoriasis in a less threatening way, and shifted his focus to improving his overall health through exercise. As participants took back the sense of power they had once given over to psoriasis and began to feel better about themselves, their psoriasis also improved, and this was central to their ongoing ability to accept it. Again, however, aspects of living with psoriasis, particularly the sense of self-consciousness it still promoted, as well as the persistent threat of its worsening, meant that acceptance was only reluctant.

Whether they had shifted from restitution or chaos, the resignation narrative involved participants finding a personally acceptable balance between the condition of their skin, their ability to keep it concealed from others and the burden of treatments and side effects in managing their psoriasis. For most participants, it involved accepting that some degree of psoriasis would always be present, that there would always be the coming and going of symptoms such as itch, and that there would always be inconveniences, side effects or risks associated with treatments. In this sense, it is a positive narrative, in that concerns with psoriasis are not in the foreground, and people are generally able to get on with living their

lives. However, as is the nature of the resignation narrative, this acceptance was begrudging; psoriasis was still viewed as a nuisance and an irritation that could impinge on daily life.

I really just got on with it.... [Researcher: So was that sort of a decision that you made, that you were just gonna...] Yeah well I, I, I tried everything I could, you know, tried different treatments that might help better, you know, and, there was nothing, there was absolutely nothing,...So that was it, you knew it wasn't going to go away, and ah, you could sort of, stop the itch, for a day, [laughs] or maybe a night, and um, that was that, yeah. (Victoria).

Despite the challenges of living with psoriasis, participants expended less focus and energy on their psoriasis compared to getting on with their lives. Further, psoriasis was not seen as linked to their sense of identity, and did not tend to shape the overall direction of their lives in a major way.

It's an irritation, and it's a nuisance, but it's not, who I am, like it doesn't affect enough of my life for it to be any kind of defining thing, about me, it's just one of those pesky things like people, like having glasses, or, it just is, um, I don't think it's, um, important enough, or big enough, for it to really sort of, mean anything, to me, it's just, an irritation and a nuisance, um I don't spend a lot of time worrying about it, I don't spend a lot of time thinking about it anymore.... (Cara).

Accepting the ongoing presence of psoriasis meant finding ways to live with it, and most participants turned to various coping strategies to help. Several trained themselves in the art of distraction from itch. Treatments were used, but with the expectation of temporary relief of physical sensations (e.g., burning, itching), or management of plaque growth rather than long-term clearance. Participants put up with the limitations of treatments for their sake of their immediate benefits.

Putting any kind of cream on it takes away the burn because it, you know, sort of cools it down, um but it doesn't last that long, um, a few hours maybe and then you've gotta wash your hair 'cause your hair's all greasy...I am yet to find a shampoo that doesn't irritate it, so you know it's just that cycle. (Cara)

The begrudging acceptance in this narrative meant putting up with psoriasis, but not necessarily embracing it in its entirety. Being able to get on with life with psoriasis required the stringent management of personal appearance; almost all participants dressed to hide their psoriasis from others, and most spoke of constantly checking whether scales had fallen on their clothes. Activities in which their psoriasis might have been visible to others were typically avoided, such as swimming, changing in shared changing rooms and visiting the hairdresser. As the power of coping strategies was limited, particularly in the realm of the psychosocial impact of psoriasis, the day-to-day impact of psoriasis remained significant, with self-consciousness, physical symptoms and the burden of treatment causing frustration and annoyance.

The awareness of it is almost worse, than the itch, because you're just constantly making sure there's no flakes and, that, I think affects me more on a daily basis than the psoriasis itself. (Cara)

Still to this day, every second day...it just builds up on my face. I have to comb out the...you know, the stuff, and exfoliate it away in a fairly vigorous way...at a certain period in that two day cycle I can't do things like eat apples or whatever, 'cause it just, you know, you stretch your face and it breaks the skin. (Logan)

One common way participants tried to develop their acceptance of psoriasis was to focus on how things could be worse than they were.

I'm very lucky really, when I, you know, I'm aware that a lot of people suffer a lot more than I, you know, I'm lucky that it didn't stay, you know, as it was in the beginning. (Jane)

My dad had psoriasis, and he had it all down his shins and quite badly on his arms and, but um, so I feel I'm quite lucky that I haven't had it as a disfiguring body, all over...and mine's been a localised one. (Victoria)

This did not necessarily minimise their personal struggle with psoriasis in practice, however.

I do know that I've gotten off lightly compared to other people but...it's still just the, you know when I'm sitting in a meeting or something and I sort of go like this and I think oh no god no what's happened, just that constant self-consciousness of having it, look, bad. (Cara)

Coping strategies were not always so positive, either. Jane spoke of dissociating from her physical self because she felt so negatively about it:

It's pretty ugly really so it makes you feel like that yourself.... I suppose it's just like the physical, um, appearance side of you as a person, you tend to, or I have, sort of set it to one side, you know. (Jane)

Participants with more severe psoriasis who were using systemic or biologic drugs expected greater management of their skin, but were also aware of the possibility these treatments might stop working for them one day.

I've tried various things and the doctor's also told me about another one whereby if it's found that the [systemic treatment] ultimately is not going to hold things back and it does get worse, he said you've gotta try it for enough time because there's some new thing which would involve injections and stuff, so. (Logan)

One participant also became concerned about the potential long-term health consequences of systemic treatments. When considering these factors, the restitution narrative resurfaced as other options for treating psoriasis were considered.

I'm hoping that, long-term, [my new dietary regime] will help my psoriasis, 'cause I know long-term, if I'm only 48 now, how many more years am I allowed to be on [systemic treatment] before I need a liver biopsy. And that's not what I want to do, 'cause they're awful. (Penny)

Herein lies a paradox of the resignation narrative, in that it is a seemingly self-empowered narrative: the person chooses to accept psoriasis and take control over their life. But this narrative can only operate so long as the severity and/or stability of psoriasis, along with any burden of treatments and/or their side effects, remain within that person's individual 'bounds of acceptance'. That is, so long as psoriasis remains at a level at which the person feels they are able to cope, which implies that the illness quietly retains ultimate control. Yet, the person is also resigned to this, and therefore, to the idea that psoriasis always retains the potential to have a more adverse effect on their life.

It doesn't worry me so much...it's just not bad, I mean, I think, if it was worse, yes, I would feel differently about it, there's no doubt about it. (Victoria)

It's not a debilitating thing you know...but I say that now because it's not like a really visible thing, but if I woke up tomorrow and all of a sudden it was um, you know like, on my forehead, or you know like, um, my elbows were covered in it...that would change the situation quite significantly. (David)

Carrie describes the fears she has around her psoriasis worsening, and, in an aspiration to a quest narrative, how she wants to use the time while her skin is relatively controlled by treatments to become stronger, so that she might be able to cope better with the psoriasis if it happened to return:

Being on [the biologic]...the relief that I've had has just, given me a space to, reflect on myself again, as a person, and build myself up, so, if there comes a time where it no

longer works for me, I won't go back to the way it was...it terrifies me that that may happen, I don't think about it because it's not here. (Carrie)

For some, age was a factor in shifting from a restitution to resignation narrative. The process of getting older brought with it a greater degree of acceptance and less concern about what others think. This allowed a greater sense of freedom to be able to go about one's life.

I could have answered things differently, probably, when I was younger.... I would have been more sort of um, positive there was a solution [laughs], I think. Now I just live with it, and make the best of it. But I think as you get older you don't worry about how you look to the same degree, and what other people think of you and, and am I a reject because I've got some disease, you don't think that when you get older...I think you just don't, well it's not that you don't care what people think, you realise it doesn't matter, but when you're young, you do, you do think about what other people think... [Researcher: You did?] Yeah, and whether you'll be accepted and thought to be unusual or abnormal. (Sally)

However, the state and visibility of their psoriasis appeared to be the overriding determining factors of whether they could sustain the resignation narrative. When psoriasis progressed outside the bounds of which a person could find ways to live with it, existing narratives were surrendered to one of chaos.

4.1.3. The chaos narrative

The chaos narrative describes a state of helpless suffering and a lost sense of life's coherence within the chaotic tumult of illness. From within chaos, the sense of cohesiveness and forward motion that are integral to narratives are impossible to achieve, which is why Frank refers to chaos as an "anti-narrative" (Frank, 2013, p. 98). Yet the decline into, experience of, and emergence from chaos can also be described retrospectively, and from this perspective, the person sharing the experience describes a time when they had become lost to illness. While not

all participants described the chaos narrative (see Figure 3 on p. 107), the extreme sense of suffering associated with chaos makes this narrative form particularly salient in considering the experience of psoriasis.

Retrospective chaos narratives were present in participants' accounts about living with psoriasis, and they followed restitution narratives that had not reached full resolution. That is, chaos occurred when hope for the successful resolution of psoriasis was abandoned, and when the stress that arose from the severity and relentlessness of psoriasis, exacerbated by other life challenges, became too much to cope with. Lacking hope and treatment options, participants could see no way in which things could improve. Two participants exhibited this narrative shift in their accounts, while a third, Logan, included more subtle references to having moved from restitution to chaos in his past. For Carrie, chaos occurred when a difficult period in her life led to an extreme flare-up of her psoriasis, and it was the experience of psoriasis itself that her chaos narrative was centred on.

Suddenly it just went boom, and that kinda scared me, I kinda wondered where am I heading, where's this going, you know? (Carrie)

In contrast, for David, the relentless presence of psoriasis was one of several triggers that wore him down over time and ultimately led to a breakdown.

I think it'd probably been chipping away at me for quite a while, just like running me down and you know, just depleting the adrenal glands or whatever you know it was just always on my mind worrying about it, so with the other things that happened, they were probably...a bit of a tipping point really, and...I basically had a breakdown...but yeah, psoriasis was part of all that, yeah. (David)

Participants described strong feelings of powerlessness in the face of rapidly worsening psoriasis and treatments that were having no effect. Both David and Carrie started experiencing new physical symptoms and felt as if their bodies that were breaking down.

... I didn't know where it was headed, and um, and I felt, too young to be going through this shit, and...I just, yeah, I didn't really know what to make of it, I tried to explain it away, and, I just thought my body was breaking down... (Carrie)

...there were other physical symptoms that became apparent to me, you know like different, like tremors and things like that, my fingers, you know, I couldn't, there was like involuntary muscle spasm and things, which, you know, um it was just a really crazy time.... (David)

A state of extreme anxiousness and fear prevailed as symptoms seemed to develop at an accelerating rate with no apparent way to halt them. Without a way of fixing their psoriasis and the inability to accept it, they felt stuck in a “vicious cycle” of stress and worsening disease.

...when it started kinda, moving along you know, I was like oh my god it's moving, it's getting worse...you know, fix it, and I couldn't, and then there's like...this internal dialogue again going on about, you know, what have I done, what have I done wrong, what am I doing to make this happen, and I really just needed to let that stuff go, 'cause that creates stress, it's like this vicious cycle you know, it um, is very difficult to get out of.... (Carrie)

All the power lay with psoriasis, which was perceived as unbeatable and as having a life of its own.

...suddenly it was behaving in ways that were just like, what the hell is this thing doing, it's like- it was like a, an entity of its own...having no control was really, is really difficult. (Carrie)

It was given so much power as to even encroach on participants' sense of identity, to the point where they were unable to differentiate between themselves and the disease.

It became part of the identity of who I, of who I was, you know? Um, I realised that, I had really, identified with, a disease, and that had become who I am, you know I'm this, I'm this ugly person... (Carrie)

I credit it with marking me in a certain way...I feel it's shaped me, ah...that's something that was, has been long-term, and it does affect how I do things... (Logan)

At one point, identity felt as if it had been lost to illness: Carrie's to psoriasis, and David's to the fear of a completely broken down body (of which psoriasis was a part) in the form of a degenerative disease. The focus on these became so great that there was very little space for anything else in life. Life as normal essentially stopped; there was no forward motion, no image of the future.

It determined, my life, it ended up determining my life including career choices you know I thought I'd never have a career, I could never go out in public, what kind of jobs can I have where I'm hidden, you know, where I can hide myself away, and yeah, it just became a focal point, of my life, so, yeah. (Carrie)

I ended up sort of, obsessing about my health, really, and psoriasis was part of it, but it kind of got to a point where there were other...physical symptoms...I jumped online and tried to diagnose what was going on with me, and uncovered all these terrible, you know, degenerative-type things, and it was just like, it just fueled, it just snowballed... (David)

Unable to control the “unsightly nature of it”, the impact of psoriasis on self-esteem and self-confidence made participating in normal activities a source of pain, that in some cases prompted people to retreat into a world of their own suffering.

Of course my self-confidence declined as the, psoriasis got worse and then when it started appearing on my face, well that was just, you can't hide that.... I reached a point where I couldn't do [normal things], and yeah, that's really soul destroying stuff,

it really gets to you and you become your own worst self-critic, because every moment of my day was really, thinking about how to hide myself. (Carrie)

...there were some days I just didn't want to leave the house, so, so, so, but I did, I did leave the house, so, you know, good on me [both laugh]. (Logan)

For both Logan and David, the development of the chaos narrative was intertwined with the experience of having psoriasis during the 'coming of age' period of early adulthood. At a time when they were trying to develop their sense of identity, particularly in social and romantic relationships, psoriasis was a major inhibitor, preventing them from feeling free to explore that side of themselves. The significance of this could be long-lasting, with one participant confiding that he had never had a meaningful romantic relationship, a fact that was clearly a source of pain for him.

That was a terrible time...yeah, for sure. Like it was a, I guess a time when you're, you know like you're living quite communally with other people...and I was quite self-conscious about, you know, like, taking my shirt off, and you know, stuff like that... (David)

...it made me very shy in intimate circumstances... (Logan)

As it was for David and Logan, extreme self-consciousness was at the core of Carrie's chaos narrative. She experienced psoriasis as debilitating, paralysing, turning her into an unlovable "monster". Carrie's desperation to escape her psoriasis led to a further kind of chaos when she decided to try systemic medications despite fundamentally wanting to avoid such extreme treatments.

The first time I was gonna put [systemic treatment] into my body I just, I was shaking, I was absolutely petrified, it was like, I was crossing a boundary between, what I believe in, and my desperation of trynna, you know, get some relief from this disease that was

just, you know felt like it was just having its way with me that I couldn't control.

(Carrie)

For Carrie, emergence from chaos was completely dependent on her psoriasis improving; that is, on a return to a restitution narrative. She described her extreme sense of desperation when she began biologic treatment:

I was um, hoping for a miracle, 'cause, I couldn't see, a future, otherwise, if my skin had stayed the way it was...I didn't know how it was going to end up, I really felt I was at a crossroads, with my life, you know, I was either gonna, turn into a very depressed person, um, hiding away from the world, surviving on a benefit, or something, um, or not surviving at all, or, some miraculous something was gonna happen, and I was gonna get my life back, so, I'm pretty, I'm pretty lucky that, you know I can inject something into my body, and it, it helps out... (Carrie)

For David, his life reached a point where he realised he needed to start taking care of his own mental wellbeing to have any hope of emerging from chaos. As he began to do so and then continued on this path, his psoriasis improved. Reaching a holding pattern – where psoriasis was maintained at a minimal level with very little fluctuation – meant that David was able to accept his psoriasis and thereby shift to a resignation narrative, yet it is clear that the holding pattern was also in part due to the positive steps he took towards accepting his situation. Similarly, part of Logan's shift from a chaos narrative to one of resignation was related to his decision to take responsibility for his general health and fitness; as his health improved, so did his feelings about himself, and so did his psoriasis. The other contributing factor to Logan's shift towards acceptance of his psoriasis was his effort to conceptualise it in ways that would help him confront it, for example, by approaching it with a sense of creativity and curiosity; this process helped him to reclaim some of the power he felt psoriasis had had over him.

Thus, in contrast to their experience of chaos, shifting to a resignation narrative meant that Logan and David had started to feel some sense of control over their psoriasis. Although they

saw little, if anything, positive arising from it, they were able to live alongside it and to actively determine the course of their own lives, rather than to feel that their lives were determined by psoriasis. At the same time, both were aware that their ability to accept their psoriasis depended on its severity staying at a certain level, and therefore the psoriasis ultimately retained the power. However, because they both had developed a sense of personal agency rather than feeling completely reliant on treatments, they were not so fearful of the possibility of psoriasis worsening.

In contrast, Carrie's need for clear skin and her perceived lack of personal agency in terms of overcoming the effects of psoriasis meant that alongside her continued efforts with treatments, she continued to live with the constant threat of chaos, and the thought of psoriasis returning invoked great fear in her. Interestingly, Carrie believed her psoriasis would improve if she were to improve her own sense of self-esteem, yet she felt powerless to do this while psoriasis was still present; hence, her reliance on treatments.

Thus, for these participants, restitution or resignation followed chaos. Although those who shifted to a resignation narrative did so by deciding to take better care of themselves, their lack of ability to find anything positive in their experiences with psoriasis sustained their sense of begrudging around psoriasis, and therefore precluded them from shifting to dominant quest narratives.

4.1.4. The quest narrative

In quest narratives, people seek to use their challenges and sufferings to create something of value. It is the only narrative of the four described here in which the person truly has agency, rather than being at the mercy of their illness or environment. In contrast to stories about other chronic illnesses, dominant quest narratives were notably absent from these stories of psoriasis. Elements of the quest narrative did feature in a minor way, in that some people felt they had developed increased empathy for others or a greater awareness of their own health and wellbeing through their experiences with psoriasis.

I guess what it's given me is a huge empathy for others, you know...just, you know, not judging people, no matter what kind of things they go through or, illnesses they have....

(Carrie)

I see people, you know, you see people round town and you know, you see their psoriasis and you think, I know what you feel. (Logan)

Yet, quest remained a background narrative as this did not appear to influence their approach to psoriasis or to their lives in any obvious way.

Aspiration towards a quest narrative in the future was also evident in Carrie's story. While in the present, she is focused on achieving clearance of her psoriasis through her use of treatments, she aspires to use her psoriasis as motivation to transform her negative self-image into a positive one, and through doing so, become a person who can offer more to the world. But this is some way off in the future; it still remains a wish, as it currently feels impossible.

While there were no dominant quest narratives in stories about psoriasis, those who also described their experience of living with psoriatic arthritis illustrated a different narrative trajectory to those found in psoriasis, one that was ultimately moving towards a quest narrative.

From chaos to resignation and the emergence of quest in psoriatic arthritis

After decades living with psoriasis, chaos characterised the diagnosis of psoriatic arthritis for the two participants who described their experience of living with it. Its diagnosis was shrouded by confusion and misdiagnosis, especially for Jane, who had been experiencing symptoms for many years beforehand. This led to feelings of being misunderstood and a hypochondriac.

I remember my [music] teacher saying about them, you know that it was quite odd the way my fingers worked, and then, you know the whole series of things really that happened, down the line, that were sort of, um, not particularly pleasant but, made me feel like I was a hypochondriac, you know I'd have, really sore, tender ribs for weeks on end and wouldn't know, what... (Jane)

Learning that it was psoriatic arthritis that had been causing their symptoms came as a great shock, made more difficult at first due to the fact that both participants had already experienced many major challenges in their lives and had had to do a great deal of personal work to get through them. The development of psoriatic arthritis felt like yet another upsetting blow, unfair because of all they had been through already. A major aspect of this was that psoriatic arthritis, with its incumbent physical limitations, threatened to take away the things in their lives that they had cultivated to bring them joy, such as movement, walking outdoors, and their other creative outlets.

[Researcher: So, with the arthritis then, how did you feel when you were diagnosed with that?] I cried.... I just thought, I...didn't want it. You know, I'd coped with the psoriasis, and I thought no, I don't want this, this is quite, something that's not going to go away, either, and, I didn't want it, I just thought, you know, I thought of those things that, I'd so enjoyed doing... (Victoria)

At first I was just all grumpy and, you know, bitter and things... I feel as though it's aged me, prematurely really, cause I've always been very youthful for my age, and now I'm sort of, you know, hobbling about [laughs], some of the time and, I've put all this weight on, which I've always been, ah, I've never been a real, um, couch potato before, and I am a bit now really... (Jane)

Medication for psoriatic arthritis helped to minimise symptoms and to therefore shift from chaos into a resignation narrative. The dependence on symptom management to maintain resignation and avoid chaos was emphasised in Victoria's story, as she struggled with finding optimal management and dosage, going from doctor to doctor. When her dose was lowered too much, she was no longer able to get on with things and the chaotic experience of pain and physical limitation returned to the foreground.

I felt pretty awful...yesterday morning, and that's when I take, the, um, painkiller and I thought oh, I just don't think I can stick another drug in my body, and I didn't take it

yesterday, and boy did I suffer, by nighttime, it was terrible...it was so painful I couldn't, move my legs in bed or my, that when I went to get out and I'm just starting to move them now, I took them, you know, as early as I could, you have to take them with food, and um, I'm starting to be able to move around a bit but, you know, that's when I realise, that, it wasn't too great, you know I have to rely on this jolly- the jolly painkillers and I don't want to, and I don't know what they do for you long-term either so, that's a little bit of a worry... (Victoria)

Both Jane and Victoria presented dominant resignation narratives in regard to their psoriasis and psoriatic arthritis, but their view of life overall was that of the quest memoir.

...once you become mature and, um, that, you have a responsibility to yourself, that's my belief, of picking yourself up, and getting on, and moving on in life, because, there's only one, there's only one life... I changed my life around, I just started to do stuff, it was hard, but I did it, and so I think, I don't think that'll leave me, you know, I'll keep, doing stuff... (Victoria)

...I think everything has um, a positive side really you know, helps you to understand other people and, helps to be able to do, you develop coping, mechanisms that you never knew you had, so, it's quite good. (Jane)

For both women, their arthritis diagnosis had occurred only about three years prior. At the time of their interviews, they were both engaged in the process of integrating their view of psoriatic arthritis into their overall view of life as a quest, in which they see their struggles as a source of value.

I feel a determination now for it not to be, the issue that I originally thought it might be... I, ah, accept the psoriasis as just being part of life really, and the, arthritic condition is, getting that way [laughs] yeah. (Jane)

Their ability to see a positive side to their struggles had been developed through experiencing trauma at a young age, and undergoing significant personal work to deal with that. Their focus tends to not be on their difficulties, but on the things that bring them joy: their creative outlets, how they can contribute and how they can help and support others. Rather than letting their arthritis stop them from doing the things they love, they are engaged with finding new ways to do them in light of their constraints.

I've always walked a lot and everything and...because I can't...still, still I plod...and yeah it's still, take a few more photographs instead of striding on [laughs]... I'm just, in the process of, almost re-educating myself to, um, approach things in a different way, you know... (Jane)

I've got, my art, but I do think, maybe, it hasn't happened yet, but I've got quite a sore thumb joint, so I have a feeling that maybe, holding the pencils won't be such a good thing but maybe I'll just get a fat paintbrush, start painting again which I haven't done for years. (Victoria)

Interestingly, unlike other challenges they have experienced in their lives, neither woman framed the psoriasis on their skin within a quest narrative. In contrast to other difficulties, psoriasis was not viewed as important enough to cause them worry, and perhaps because of this, it is not seen as 'big' enough to transform into something meaningful. The personal work they had undergone helped them to reach a place of self-acceptance, and so psoriasis was seen more as a surface affliction rather than as something that could affect them at a fundamental level. At the same time, both participants' psoriasis was relatively stable, whether due to medication for psoriatic arthritis or to a natural reduction in symptoms, which also minimised the amount of suffering it brought about.

In summary, participants predominantly described their experience of living with psoriasis using Frank's restitution and chaos narrative forms, and through the resignation narrative. The restitution narrative remained unresolved due to the difficulty in treating psoriasis, yet provided

a sense of hope; chaos was characterised by a sense of powerlessness and suffering; and resignation involved a begrudging acceptance and a focus on getting on with life. Shifts between narrative forms occurred over time, with preeminent factors in these shifts being the perceived severity and stability of psoriasis, including its response to treatments. While dominant quest narratives were not apparent in experiences about living with psoriasis, those for whom psoriatic arthritis was a major part of their story described a different narrative trajectory in relation to this condition, shifting from chaos to resignation, with quest narratives beginning to emerge at the time of the interviews.

Having presented the findings of this research into the experience of living with psoriasis, this thesis will now turn to a discussion of the meaning of these findings, within the context of the wider literature.

4.2. Discussion

Participants' narratives and the narrative forms that they take provide insight into the way people understand their experiences with psoriasis. The predominance of restitution, resignation and chaos narratives indicate that psoriasis can be seen as a temporary condition that must be overcome, a burden that must be endured, or a force that is overpowering, respectively. The use of these narrative forms demonstrates the challenge in accepting the permanency of psoriasis and the need to sustain hope for the future, the struggle to find ways to manage it, and the ongoing imposition psoriasis has on a person's life regardless of his or her degree of acceptance. In all narratives, psoriasis was seen as maintaining some degree of control over people, in that its relative severity and stability determined whether or not they could get on with their lives in a state of comparative normalcy. When psoriasis could not be managed, people felt helpless and were thrown into turmoil. Fluctuations in psoriasis, and changes in other personal and life circumstances, meant that the experience of psoriasis continued to shift and evolve over the course of people's lives, and shifts between narrative forms followed accordingly. The experience of psoriatic arthritis followed a different narrative trajectory, with the period following diagnosis the most challenging due to the severity of the symptoms, their immediate impact on physical functioning and the question of what having the condition might mean for the future. Attaining adequate management of psoriatic arthritis promoted some degree of acceptance, and the already-established positive life views of those participants in this study allowed them to begin seeking new ways to live alongside their condition.

4.2.1. The persistence of the restitution narrative in the face of no cure

Participants told prolonged restitution narratives in the years that followed the onset of psoriasis because the alternative – having psoriasis for the rest of their lives – was seen as unacceptable. This stemmed not only from a natural desire to return to health, but also from the belief that a cure or effective treatment must exist, and from the sense of intolerability that surrounded living with the many implications of psoriasis. These factors meant that the idea of achieving clear skin, and thus 'returning to normal', was made a central focus, despite participants being aware

that psoriasis had no cure and that full clearance was unlikely.

While the possibility of attaining clearance of severe psoriasis has increased since the development of biologic treatments (Strober et al., 2016), for most participants, the many years of the restitution narrative corresponded to a time prior to biologics and when clearance was considered an unrealistic expectation (Al-Suwaidan & Feldman, 2000). Even today, the estimated proportion of people who achieve full clearance of psoriasis is very small (Boehncke & Schön, 2015). Furthermore, biologic treatments are expensive, and thus accessible only by those with more severe psoriasis and for whom other treatments have proven ineffective or intolerable (Berth-Jones, 2013; My Psoriasis, 2015). Although Frank (2013) suggests that restitution narratives are used infrequently in those with chronic (as opposed to acute) illnesses, as their prognosis does not typically involve a complete return to health (Bury, 1991), the use of restitution narratives in people with psoriasis emphasises that the likelihood that a return to health might never occur does not preclude people from seeking it. This point is supported by the use of dominant restitution narratives in people with other chronic illnesses such as human immunodeficiency virus (Ezzy, 2000), breast cancer (Thomas-MacLean, 2004) and chronic fatigue syndrome (Whitehead, 2006), and in those living with the disabling consequences of stroke (France et al., 2013) and spinal cord injury (Smith & Sparkes, 2005). As most people who are ill naturally want to be well again, the hope for restitution could therefore be considered a normal part of any illness, whether acute or chronic. What is notable about the prominence of the restitution narrative in the experience of psoriasis are the large efforts people made in their search for effective treatments, and the length of time over which this persisted, even though they had received medical advice about the incurability of psoriasis and limitations of its treatments.

Because the idea of long-term or life-long psoriasis was seen as unacceptable, at the core of the restitution narrative was a strong need for hope that psoriasis could be overcome. In the initial years of living with the disease, participants forged hope through either disregard of or disbelief in what they had been told about psoriasis: that it had no cure and that treatments might never

clear it. In this sense, hope can be seen as deriving from a wider cultural belief that every illness must have a corresponding cure (Frank, 2013). The need for hope increased as time went on and the many implications of psoriasis became more apparent, such as its high management demands and consequences for confidence and self-esteem. Hope for a return to clear skin provided some counteraction to the sense of intolerability about living with these ongoing consequences of psoriasis and worry about what they might mean for the future. This need to sustain hope for a return to a prior state of health has been similarly expressed by others living with chronic illness or disability, such as men who had become confined to wheelchairs due to spinal cord injuries (Smith & Sparkes, 2005). Just as many of these men held onto the hope of being able to walk again, as this hope was the means by which they could get through each day, those with psoriasis expressed the need to hold onto hope for a return to clear skin as they grappled with the daily realities of living with the disease.

While hope is generally considered a positive attribute, hope that prolongs a restitution narrative over time may ultimately prevent people from adjusting to and accepting their psoriasis. Using the concepts put forth by Dufault and Martocchio (as cited in Fitzgerald Miller, 2007), hope for restitution can be described as *particularised* hope, as it is directed towards a specific goal, and this contrasts with *generalised* hope, which refers to an overall state of being that enhances life and protects against despair. Pinning hope on the outcome of clearance when this is difficult to achieve, especially in people without access to more advanced treatments (Boehncke & Schön, 2015), could lead to an all-consuming, endless search for an effective treatment and a near-obsessive treatment effort that only provides temporary relief. On one level, this can be illustrated by the considerable time and effort that people put into applying treatments in the hope that they will provide clearance; hours and energy that could be otherwise used for living life. On another, a person's beliefs about what might have caused his or her psoriasis, or what might cure it, can lead to a major fixation on that aspect of life. For example, the influence of specific dietary types in causing or curing psoriasis was suggested numerous times during interviews, with recent media-driven dietary trends often providing new avenues for hope, but

with the theories behind these trends and the efforts to implement dietary changes also becoming a central and dominant focus of people's lives.

Hope for clearance that is unlikely to be achieved can also mean extreme disappointment when this hope is not met. In some cases, participants interpreted doctors' prescriptions of treatments as implicitly providing hope. As these were not always accompanied by a clear indication of their potential limitations, a shortcoming that has also been noted in previous research (Bewley et al., 2014), they carried with them the inherent message that their use would lead to an improvement in psoriasis. Yet, this led to disappointment once a person came to their own realisation that nothing would work after all treatment options were exhausted, and a lot of time, energy and money had been expended on them. On the other hand, doctors who offered no sense of hope at all were not well received, as a complete lack of hope could be similarly devastating; participants described needing to generate a sense of hope for themselves to avoid feelings of futility. This has clinical implications in the sense of the importance of empathetically and carefully managing a patient's need for hope in the face of psoriasis, while offering a realistic idea of the limitations of treatments.

Participants differed in the extent to which they rejected the concept of there being no cure for psoriasis. Some participants seemed to accept this on some level, yet they sought permanent clearance regardless, while others directly rejected the idea. This difference can be considered in terms of having "hope-as-want", where participants desired clearance but knew it was unlikely, or having "hope-as-expectation", where they anticipated being able to achieve permanent clearance of psoriasis (Wiles, Cott, & Gibson, 2008). Yet, even when the chance of clearance was thought to be slim, this did not prevent people seeking it. Some participants also began with the expectation of clearance, which then became more of a wish as time went on and their certainty around overcoming psoriasis lessened.

4.2.2. Loss of control, identity and the chaos narrative

When psoriasis progressed beyond a person's 'bounds of acceptability' in terms of acute severity or due to its persistence at a certain level over time, and there was no remaining hope for overcoming it, people felt powerless in the face of their psoriasis and hopeless about the future, as was illustrated by a shift to the chaos narrative. This particularly related to the inability of participants to keep psoriasis hidden from others coupled with a high level of sensitivity to others' judgments, and to a feeling that their bodies were breaking down. In this sense, participants experienced a feeling of having lost control over their bodies, which was also apparent in reference to their near-obsessive, but unsuccessful efforts to minimise the proliferation of scales shedding from skin or the encroachment of lesions upon exposed skin. While feelings of having lost control over one's body had occurred to some degree at the initial onset of psoriasis, at that time these were mitigated by the hope of restitution, and furthermore, such feelings were not so intrusive when psoriasis was more minimal or stable. In chaos, a person did not just feel that they had lost control, but that they had been overtaken by psoriasis. It was seen as having forcefully imposed itself on them over time or having uncontrollably escalated in severity, and had also taken away aspects of their lives that they had previously taken for granted, such as having 'normal' skin, and a sense of stability and predictability about their body.

A body that feels excessively unpredictable and out of control engenders a sense of powerlessness (Makarem, Smith, Mudambi, & Hunt, 2014), which has an adverse effect on a person's self-image and sense of identity and thus leads to a diminished sense of self (Charmaz, 1983). It follows then, that feeling as if their bodily control had been conceded to psoriasis led some participants to also feel that they had lost their sense of personal identity to psoriasis. To illustrate, one participant described how even when her psoriasis was minimal, the smallest spot seemed magnified so that she could not see herself for her psoriasis, and she also believed that this was how she was seen by others. Feeling defined by psoriasis had profound consequences, as it meant that options that would normally be open to a person, such as finding a job, having a

relationship, and even being comfortable leaving the house, were seemingly closed off, as psoriasis seemed to claim every last bit of self-confidence. While difficulties around these aspects of life were also described within the context of other narrative forms, from the perspective of the chaos narrative they appeared impossible. Living an increasingly isolated and restricted life as a consequence of feeling shame about the appearance of skin further compounded a sense of identity being lost to psoriasis. As Charmaz (1983) argued, a life that is severely restricted by illness fosters an “all consuming retreat into illness, and under these conditions, illness structures...worlds and shapes...self-concepts” (Charmaz, 1983, p. 175). This also describes the impact of the physical limitations that developed with the onset of psoriatic arthritis. Not only did arthritis threaten people’s sense of identity through a loss of predictability and control over their bodies, but its physically restrictive symptoms also took on wider meaning in that they threatened to take away aspects of people’s lives on which they had built their sense of identity, such as their physical fitness and creative pursuits. Paradoxically, at the same time that identity became lost to psoriasis, a still-present self judged oneself to a debilitating degree because of the skin’s appearance. For instance, the same participant described above found it impossible to fathom how her psoriasis was not a problem for her partner, and she felt guilty for being a “monster” with rough, unsightly skin. This judgment contrasts with that in other narratives, which was frequently directed at one’s own appearance, but did not extend to the level of self.

Participants’ emergence from chaos was linked with their efforts to gain a sense of control, and thus hope, back in their lives. This occurred in different ways for different participants. Carrie’s shift from chaos to a restitution narrative illustrated her need to try and gain control over her skin, in order to feel control over her life and hope for the future. In contrast, for David and Logan, shifting to a resignation narrative demonstrated that their focus was foremost on taking action to gain control over their lives – and their skin naturally improved as a consequence. What triggered each of these participants to make such efforts seemed to be reaching such a low point – ‘rock bottom’ – that there was nowhere else to go but up. Interestingly, David and

Logan's shift to the resignation narrative showed they had reached a degree of acceptance with regards to their psoriasis, yet acceptance remained out of reach for Carrie. This may relate to the different manner in which they sought to emerge from chaos, with Carrie's renewed hope still pinned on achieving clear skin, whereas the hope of the others was directed at a future lived well with psoriasis. It may be that through making efforts to take care of themselves and seeing a corresponding improvement in their psoriasis, David and Logan shifted towards a more internalised sense of control around their health, whereas the lack of improvement in Carrie's skin, despite her efforts, left her feeling personally powerless over her psoriasis. This differentiation is important, as those who feel a greater sense of control over illness have been found to have lower levels of distress, increased positive self-image, and to focus less on restrictions imposed by the illness (Makarem et al., 2014). On the other hand, although Carrie felt unable to personally influence her psoriasis, her eventual success with biologic treatment enabled her to feel a greater sense of control over daily life through no longer having to deal with the stresses of psoriasis. Similarly, in participants with psoriatic arthritis, their shift from a chaos narrative to one of resignation showed how finding a medication that minimised their physical symptoms helped them to gain a feeling of greater day-to-day control following their diagnosis. However, in contrast to Carrie's experience of emerging from chaos, these participants shifted to a resignation narrative, illustrating their begrudging acceptance of having psoriatic arthritis, rather than renewed efforts to seek out a way to overcome the disease, as they realised the only way they would be able to move forward was to find a way to live with it.

4.2.3. The resignation narrative: Acceptance that is at most, begrudging

A shift to the resignation narrative was driven by the realisation that psoriasis was unlikely to improve to any great extent, and by the desire to get on with one's life without the predominant focus being on psoriasis. It therefore followed either an abandonment of the restitution narrative when hope for clearance was relinquished, or an emergence from the chaos narrative based on a desire to feel some control back over one's life. Yet, acceptance of psoriasis was only possible when it was seen as relatively stable and concealable, and at a level of severity

that a person felt they could live with. Participants accepted that there was little hope for full clearance, and acceptance allowed them to begin focusing on getting on with life. This acceptance, however, was of a reluctant, begrudging nature, as psoriasis was still perceived as a negative imposition that would always be associated with some degree of challenge. That this narrative, with its begrudging undertone, was the most positive dominant narrative form used in participants' stories suggests the ongoing difficulties people experience as a result of living with psoriasis.

Despite the realisation that some degree of acceptance was required in order to get on with life, a shift to a resignation narrative did not necessarily correspond to an improvement in the day-to-day implications of living with psoriasis. In fact, the difficulties around having to deal with the presence of psoriasis on an ongoing, daily basis was at the core of the sense of begrudging surrounding the acceptance of psoriasis. The body plays a central role in the formation of social identity (Öberg & Tornstam, 1999), and this explains participants' fears of negative social evaluation because of the appearance of their skin, and their hypervigilance towards trying to maintain their appearance in an attempt to manage the impression that they made to others (Kent, 2000). In support of the proposition made by Leary and Kowalski (1997), the more difficult they felt it was to keep their psoriasis hidden from others and therefore manage their appearance, the greater the sense of self-consciousness and anxiety they seemed to feel in relation to social settings. Such hypervigilance also prevented people from giving their full attention to other aspects of life, and was mentally draining over time. Flaking skin from the scalp presented a particular problem, as it seemed essentially impossible to avoid scales becoming visible in hair or falling onto clothes.

Similarly, a shift to the resignation narrative did not always mean being absolved of the need to treat psoriasis, and the inconvenience and hassles related to treatment use further contributed to the sense of begrudging. Using topical treatments still felt like a perpetual, burdensome task due to the effort required, and because they typically provided no more than temporary benefit, while the risks and side effects of systemic treatments also added a considerable sense of

burden. This is despite participants having minimised their treatment use as much as possible, and routinised them as a part of daily life over decades of living with psoriasis. Yet, treatments were still seen as necessary, as the alternatives of intense itch or a build-up of scales, and sometimes a spread of plaques, were usually perceived as even less desirable. Furthermore, the ongoing use of treatments contributed to a sense of relative control over psoriasis. While participants could not feel as if they had complete control over their psoriasis because they lived with the ongoing awareness that it could worsen, they were able to feel they were playing an active part in the management of these symptoms by creating a process out of the routinisation of applying or taking treatments, filling prescriptions and attending doctors appointments, which is reminiscent of the relationship described between these factors and the ability to adjust to psoriasis by participants in Uttjek et al. (2007).

This desire for control over symptoms was also prompted by social expectations around the treatment and management of illness. As Jobling and Naldi (2006) point out, unlike for other chronic illnesses which tend to invoke a degree of public empathy, the chronicity of psoriasis and other skin diseases can be socially interpreted as an inability to adequately manage or control the condition – as if it is a failing on the person’s behalf. This attitude was even present amongst those with psoriasis, as illustrated by one participant who had observed a passerby with severe psoriasis and noted, “they’re doing nothing with [their psoriasis]...it’s just been left”. Such a perspective is representative of the neoliberal ideology that maintaining one’s good health is the sole responsibility of the individual, and the outcome a result of the choices they do or do not make (Galvin, 2002). ‘Ideal citizens’ are considered to be those who can maintain an optimal state of health; because, as Leichter argues, “[health] symbolises a secular state of grace. As such, good health constitutes affirmation of the life lived virtuously” (as cited in Galvin, 2002, p. 116). By extension then, those who are unable to sustain good health, such as those who are afflicted with chronic diseases such as psoriasis and unable to control them, are seen as unworthy, and even a failure on moral grounds (Galvin, 2002). While the difficulty in overcoming psoriasis prohibits the full attainment of ‘virtue’ within this paradigm *via* a

complete return to health, persistence with treatments allowed participants to feel that they were at least partially fulfilling social expectations that they should ‘do something about’ their skin condition.

Intuitively, the resignation narrative form feels like it must be commonplace amongst sufferers of chronic conditions, underpinning the stories of those who struggle with the reality of their illness or disability but have the desire to not let it dominate them or their ability to live life. Surprisingly however, a post-analysis examination of the literature identified only one other study in which a comparable narrative was described. In experiences of aphasia, a condition where language is impaired following stroke or other brain injury, participants used narratives of ‘acquiescence’, where the plot line involved “an emerging and culminating feeling of stability and acceptance” yet often with a negative tone (Mitchell et al., 2011, p. 326). Aphasia is similar to psoriasis in that it is a non-life-threatening, yet chronic condition that can have a significant, negative day-to-day and psychosocial impact (Mitchell et al., 2011), and it is these characteristics that likely supported the development of the resignation (or acquiescence) narrative in people’s experiences. Thus, the lack of narratives in which a begrudging acceptance of illness is found may relate to the limited number of narrative analyses that have been conducted into the experience of illnesses with similar characteristics. On the other hand, the resignation narrative does share some similarities with the way that some others have understood Frank’s ‘quest memoir’ narrative. Frank describes this form as the “gentlest” of the quest stories, where “trials are not minimised, but they are told stoically, without flourish”, and “no special insight is claimed at the end; the insight is rather the incorporation...of illness into the writer’s life” (Frank, 2013, p. 120). Thus, some authors (e.g., France et al., 2013) have identified a narrative as a quest because it is focused on acceptance of illness and the effort to get on with life – elements that are also key parts of the resignation narrative. However, they also note an overall positive, accepting attitude towards illness, which differs from the begrudging tone of resignation that was identified in this study and is a key feature of the resignation narrative.

4.2.4. Narrative trajectories and the role of perceived stability and severity of psoriasis

Rather than being limited to a single narrative form, the experience of psoriasis involved shifts between different narrative forms over time that together, established an overall narrative trajectory. The perceived stability and severity of psoriasis, its degree of visibility, and how these related to an person's beliefs around what they were personally able to manage, had a strong influence on how people experienced psoriasis over time, and thus on the narrative forms they used and the narrative trajectory that unfolded for each person. In the restitution narrative, hope for clearance and the seeking of treatments were driven by a sense of intolerability towards psoriasis as it was manifest. In resignation, the relative stability and severity of psoriasis, the extent that it was visible, and the burden brought about by treatments all remained at a level that the person felt able to manage and accept. In chaos, the severity and/or stability of psoriasis and the ability to manage its appearance had exceeded the bounds for which acceptance was possible. In a study of the lived experience of people with severe psoriasis, Wahl et al. (2002) also found that the severity of symptoms and flare-ups were key factors in whether the participants felt they were coping or not coping; here, 'not coping' referred to a state of extreme suffering that can be reasonably equated to the chaos narrative.

As psoriasis tends to be unpredictable by nature (Menter et al., 2008a), the relevance of disease stability and severity in influencing the experience of psoriasis is of particular importance. It suggests that a person's acceptance of psoriasis is always conditional upon psoriasis remaining at a level that they perceive to be acceptable, outside of which people either return to a restitution narrative and refocus on overcoming it, or shift to a chaos narrative, experiencing feelings of powerlessness and hopelessness. The idea of psoriasis as something unpredictable was evident in the present study, as even in those whose psoriasis had been relatively stable for some time, their experience of fluctuations in the past meant that they saw their psoriasis as having the potential to worsen in the future. Further, even participants who had identified specific triggers for flare-ups of their psoriasis could not escape the sense of unpredictability, as these triggers did not explain all of the fluctuations of their psoriasis, and many of them (such as

stress, sweat, sunlight and winter) were almost impossible to avoid. That psoriasis is inherently unpredictable, and that perceived psoriasis severity plays a central role in influencing the experience of psoriasis therefore highlight the sense of precariousness around living with the disease. Fluctuations in psoriasis can mean that people similarly fluctuate between the resignation narrative, and thus the ability to somewhat accept it, the restitution narrative and the need to overcome it, and the chaos narrative, and the feeling of being at its mercy.

Considering narrative forms and overall trajectories captures how actions, perspectives and happenings do not occur in isolation, but are instead contingent on each other and as such, form an overall story. In this sense, the order of experiences, and therefore narratives, is important in the construction of a person's overall narrative trajectory. To illustrate, for some people, the resignation narrative followed the abandonment of hope for clearance and/or cure as they accepted that psoriasis treatments only offered temporary relief, and in some cases were more hassle than they were worth. For other people, the shift to a resignation narrative marked the beginning of being able to get on with life following their emergence from a chaotic state of despair. In the different narrative trajectories (in this case, from restitution to resignation, or from chaos to resignation) the latter narrative takes on a different meaning in each situation. The difference between these trajectories can be considered in terms of Bury's influential concept of "biographical disruption" (Bury, 1982), which describes the onset of chronic illness as disrupting assumptions about one's body, self and life that have previously been taken for granted. In the different narrative trajectories, biographical disruption occurs to different degrees. In trajectories that followed the shift from restitution directly to resignation, for example, psoriasis is pushed to one side as the focus returns to living one's life in the same way as before, as best as one can. In this case, psoriasis has had limited impact on a person's ongoing sense of self, and thus biographical disruption has been minimal. In contrast, those who have experienced chaos and then shift to a narrative of resignation do so having experienced major biographical disruption; they have experienced a world of suffering, and have changed at some fundamental level as a result. They emerge from chaos having

experienced the feeling of their sense of predictability and control over their bodies – in fact, all the things they took for granted – having been lost to psoriasis, and even more, they have felt it claim their self-esteem and sense of identity (Charmaz, 1983). The relative sense of freedom and the apparent power of choice in the resignation narrative is therefore made all the more meaningful because of having experienced the powerlessness and hopelessness of chaos. This impact of prior experiences on those that follow emphasises the importance of considering the narrative trajectory, and thus a person’s long-term experience of illness, as a whole.

4.2.5. Consequences of the incongruence between psoriasis and societal ideals around appearance

Fundamental to the sense of begrudging in the resignation narrative, the need for hope in the restitution narrative and the overwhelming hopelessness of the chaos narrative, was the incongruence between the appearance of psoriasis and societal ideals around personal appearance, as well as the overall emphasis on appearance in how people are defined and judged. The societal context within which these narratives are told is one in which great emphasis is placed on both personal appearance and health, and relatedly, in which smooth, healthy skin is idealised (Öberg & Tornstam, 1999; Rumsey & Harcourt, 2004). The perpetuation of these ideals, for example through circulation by the media, ingrains them so that they become cultural ideals, and members of society are expected to conform to these ideals (Livneh, 1982). Those who deviate too far from the norm, such as can be said for those with psoriasis and other skin conditions, are often stigmatised as a result of their differences (Phemister & Crewe, 2004), which undoubtedly makes it all the more difficult for people to accept that they must live with these differences. Relatedly, many with psoriasis believe that other people see their skin to be ugly, unclean and/or infectious (Bewley et al., 2014; Magin et al., 2009a). As discussed earlier in this thesis, such disparaging views have been considered a projection of what the person with psoriasis thinks about him or herself onto others (Wahl et al., 2002; Khoury et al., 2014), and there is evidence that many people in the wider population do also hold these beliefs (Donigan et al., 2015). Some of the participants in this study described

overt and painful experiences of social discrimination based on this divergence in appearance, which caused them to feel shame and reinforced both their need to hide their psoriasis and the overall sense of difficulty they felt towards living with the disease.

In comparison to being the subject of reactions from others, participants' judgments of their own appearance appeared to be a more prominent contributor to the sense of begrudging in resignation, the need to seek restitution, or to the despair of chaos. This judgment appeared to arise from a keen awareness by participants that their psoriasis prevented them from conforming to society's expectations around appearance. Participants were overly worried about how other people viewed them because they had personally internalised societal standards around appearance and made them their own. Focusing on the visible differences between themselves and others brought about by their psoriasis, they considered themselves as outsiders; one participant mentioned her wish that society could re-define 'normal' so that it did not exclude those who looked differently to others, but this was seen as wishful thinking. With the cultural importance placed on appearance seen as essentially impossible to change and also internalised within the self, the resignation narrative involved begrudgingly accepting feelings of being different to others. In contrast, restitution was sought because it was the only means by which people felt they could regain the sense of 'sameness' in appearance that would allow them to stop feeling like an outsider, and when chaos occurred, it was due to an inability to cope with such feelings.

4.2.6. The challenge of creating value from psoriasis: The lack of quest narratives

There was a notable scarcity of quest narratives about living with psoriasis in the current research. No participants felt that their life had been particularly positively influenced as a result of having psoriasis, and in those who mentioned that it had brought them a greater sense of empathy, this was overshadowed by the ongoing negativity they associated with the disease. Similarly, previous research into living with psoriasis has indicated that for most people, the experience is an overall negative one, with the considerable social and emotional consequences

of psoriasis fundamentally contributing to this (Krueger et al., 2001; Nash et al., 2015; Anstey et al., 2012). In contrast, Fortune et al. (2005) have suggested that some people with psoriasis might experience “adversarial growth”, where they attain fundamental benefit or personal growth as a result of undergoing difficult life circumstances. However, methodological limitations of the research conducted to determine whether this was the case prohibit any firm or detailed conclusions about personal growth in psoriasis, as not only was assessment based on answers to only four questions, but it only related to change in personal growth, and over a timeframe of just six months (Fortune et al., 2005).

While it might seem logical that in general, people struggle to find a positive side to living with illness, in fact, there are countless examples of those who have viewed their experience of illness in an overall positive light due to the value they created from that experience. These include experiences that aligned with the quest narrative itself, which have been ubiquitous amongst those who have experienced suffering and trauma as a result of various illnesses or disabilities, including breast cancer (Thomas-MacLean, 2004), stroke (France et al., 2013), human immunodeficiency virus (Ezzy, 2000), chronic fatigue syndrome (Whitehead, 2006) and spinal cord injury (Perrier, Smith, & Latimer-Cheung, 2013; Smith & Sparkes, 2005). Participants in these studies all describe having gained a new perspective on life as a result of their painful experiences, and having undergone positive personal transformations. In contrast to the prevalence of the quest narrative amongst experiences of other illnesses, just one study has illustrated that is possible for psoriasis to be used to create positive meaning for one’s life in a manner akin to the quest narrative. In their consideration of the relationship between psoriasis and the self-concept, Watson and de Bruin (2007) described how after living with psoriasis over many years, participants had found greater meaning in their lives as a result of having had psoriasis, due to using psoriasis as a tool to reclaim their lives and rebuild themselves anew. Their experiences of trauma as a result of psoriasis – what have been described in the present study as chaos – meant that they would be forever shaped by their psoriasis and experiences, but they had used this trauma as a catalyst to bring forth a new, stronger and more resilient self

(Watson & de Bruin, 2007). What is common to the narratives in these studies is fundamental to quest narratives in general: that the creation of positive meaning from illness or disability occurred as a result of having undergone suffering and then emerging from it, and from looking back and reflecting on that suffering. As people frame their experiences according to different narrative forms, thereby enabling them to make sense of those experiences (Bruner, 1990), the quest narrative represents the ability of people to understand their experience as something that offers them the potential to grow and to create value.

It follows then, that the degree of suffering that a person undergoes will likely influence the way that people make sense of their experiences, and thus the narrative forms that underpin them. It is possible that for some participants in the present research, the suffering caused by psoriasis was not to such an extent that it could be constructed as a catalyst for fundamental personal change. Indeed, some participants described psoriasis as a “nuisance” and a “bother”, but had not let it interfere with their life in any great way, nor with their sense of self. On the other hand, as mentioned above, there is some suggestion that several people who had undergone chaos because of psoriasis or psoriatic arthritis were gradually orienting themselves towards quest narratives in the future. Particularly in the narratives of Carrie and Logan, who had undergone great suffering as a result of their experiences with psoriasis and its impact on their identities, there was the sense that a different narrative might be told if they were to be interviewed again in the future. In fact, Carrie verbalised this in her hope that she could use psoriasis to grow as a person, whereas Logan’s ongoing efforts to accept his psoriasis were reflected in a gradually increasing acceptance of himself. Yet, neither Carrie nor Logan had yet reached a point where they were able to reflect on the past without some degree of pain. As psoriasis was still understood in a negative light, their ability to find value in their experiences was limited.

This raises a second important point with regard to the lack of quest narratives found in the present research, that the narratives of people are necessarily unfinished, for as long as they continue to live (and in some cases, even after their passing), their story continues to unfold

(Polkinghorne, 1988). Thus, the lack of quest narratives amongst participants in the current research must first be considered as a condition of the present; these narratives are of a certain point in time, and the narrative of the future is as yet untold. As Frank noted, the “notion of reliability – getting the same answer to the same question at different times – does not fit here. Life moves on, stories change with that movement, and experience changes” (Frank, 2013, p. 22). The change that usually occurs with the passing of time can bring with it shifts to new narrative forms that are as yet unknown in the present. Taken together, these points suggest that particularly in those who have experienced the great suffering of chaos, there is the potential that the passing of time and the required degree of self-reflection may lead to the use of a quest narrative in the future.

4.3. Conclusion

In conclusion, the different narratives that people used to describe their experiences with psoriasis, and the various narrative trajectories they followed, demonstrate a number of ways that people experience life with the disease, and show how the experience is inextricably linked with the degree to which people feel they can manage their psoriasis and its visibility to others. The narratives identified through this research explicate how participants’ experiences of psoriasis variously involved an often-consuming pursuit for clear skin, a sense of helplessness, powerlessness and despair, and a sense of begrudging acceptance. The overall tone towards psoriasis was negative throughout these narratives, and at its most challenging, psoriasis dominated people’s sense of identity. Unlike in experiences of other chronic illnesses, there was a distinct lack of dominant quest stories, reinforcing the idea that people have difficulty accepting psoriasis and deriving positive meaning from it.

The broader implications of these findings will be discussed in the final chapter of this thesis (Chapter 7). In the meantime, they provide further support for the need to identify an effective, safe and convenient treatment option for psoriasis. The difficulty in managing psoriasis was a central element of the narratives, and thus how people experienced living with psoriasis. The

extended search for an effective treatment in the restitution narrative, the reluctance that accompanied acceptance of psoriasis in resignation, and the perceived loss of control in chaos all arose because of the ongoing challenges surrounding the treatment and management of psoriasis. From another perspective, reaching a point of acceptance with psoriasis in the resignation narrative, although it was of a begrudging nature, only appeared to be possible because psoriasis was seen as being relatively stable and under control. These factors were therefore central to people feeling they were able to live alongside their psoriasis, rather than being focused on the need to overcome it or feeling dominated by it.

Thus, with these findings in mind, this thesis will now shift to addressing its second aim, to determine whether an effective treatment for psoriasis may be found in oral vitamin D₃ supplements. If these were found to improve psoriasis, they would offer a highly convenient treatment option that is free of side effects and risks.

5. Study Two: Assessing the Efficacy of Vitamin D₃ Supplements for Treating Psoriasis

The previous chapter considered how people experience living with psoriasis, and determined that the nature of experience is intertwined with people's perceived ability to manage and treat their psoriasis. The focus of this chapter is to provide the background, methodological approach and methods for the research presented in the following chapter (Chapter 6), which is based on the aim to determine whether a safe and effective treatment for psoriasis is found in oral vitamin D₃ supplements. With this shift in focus also comes a shift in epistemological perspectives, from one where meaning is constructed through people's interactions with the world around them, to one where meaning is found in the object or phenomena. To give a specific example of the latter in relation to the research presented and discussed in this chapter and the next, the administration of oral vitamin D₃ raises circulating vitamin D (calcidiol) levels, and this is objectively accepted as factual.

This chapter presents a critical discussion of the evidence linking vitamin D and psoriasis, to provide a rationale for the importance of investigating vitamin D as a treatment option, and this is followed by details of the methods used to conduct this research. Firstly, however, the chapter begins with a detailed introduction to vitamin D, in order to clarify what vitamin D is, how it is metabolised and how it functions within the body, and to discuss the optimal intake and blood levels, all of which are necessary to understand prior to an investigation into its efficacy for treating psoriasis.

5.1. Vitamin D

5.1.1. Background

From the 19th to early 20th century, it was hypothesised and then determined that a lack of sunlight exposure led to rickets, a bone-deforming disorder in children, and that helio- and phototherapy enabled its prevention and treatment (Holick, 1995). Since then, vitamin D has been inextricably linked with bone health and calcium absorption, and much of the focus of

vitamin D research throughout the earlier 20th century was on understanding this role. Less well known is that the modern day association between vitamin D and psoriasis began around the same time, also with the advent of phototherapy. In 1903, Niels Ryberg Finsen was awarded the Nobel Prize for his observation that lupus vulgaris, a bacterial infection of the skin associated with tuberculosis, could be treated with phototherapy (Hönigsmann, 2013). Twenty years later, William Goeckerman developed a mercury arc lamp that emitted UVB light, specifically for the treatment of psoriasis (Hönigsmann, 2013). In the decades following the development of Goeckerman's lamp, the successful use of high doses of oral vitamin D₂ in lupus vulgaris was to be the inspiration for a group of dermatologists to try the same regime in psoriasis patients, reasoning that since both psoriasis and lupus vulgaris responded to phototherapy, then so too might psoriasis respond to oral vitamin D (Kindler, 1949). Since these early studies, which produced mixed results, investigations into the association between vitamin D and psoriasis have taken several forms.

The purpose of this review is to examine this association and to critically consider the evidence supporting a potential benefit of oral vitamin D₃ supplements for psoriasis. It will begin with presenting relevant background information on vitamin D, including its types and sources, metabolic pathways, physiological functions, factors affecting vitamin D status and response to supplementation, and definitions of vitamin D status and optimal intake.

5.1.2. Definition of vitamin D

Contrary to its name, vitamin D is not a vitamin. Unlike for true vitamins, the major source of vitamin D is not dietary intake but exposure of skin to sunlight. Rather, vitamin D is better described as the precursor to a hormone, that being calcitriol, the active form of vitamin D (Thacher & Clarke, 2011). Calcitriol meets the definition of a hormone in that it is synthesised in specific cells in the body, and acts in an autocrine, paracrine or endocrine manner on target cells to change their functioning (Thacher & Clarke, 2011).

5.1.3. Physiological functions of vitamin D

Maintaining calcium and phosphate homeostasis, and relatedly, the mineralisation of bone, are the canonical functions of vitamin D (Thacher & Clarke, 2011). However, the past fifty years has seen a great expansion in understanding of the wider significance of vitamin D for the human body, as it has emerged that essentially every cell and tissue possesses a vitamin D receptor (VDR), and thus has the potential to respond to vitamin D (Holick, 2008b).

It is thought that more than 200 different genes are regulated through the VDR (Holick & Chen, 2008). These genes are related to bone, mineral, detoxification, cell life (proliferation, differentiation, migration and death), immune, and metabolism (amino acid, lipid and carbohydrate) (Haussler, Jurutka, Mizwicki, & Norman, 2011). Thus, vitamin D plays an active role in some of the most essential processes in the human body (see **Figure 4**).

5.1.4. Forms of vitamin D

Vitamin D exists in two forms, D₂ (ergocalciferol) and D₃ (cholecalciferol), both of which can be found and similarly utilised within the human body (Thacher & Clarke, 2011). Vitamin D₂ is produced when UVB reacts with a substance called ergosterol in cell membranes of plants and fungi (Holick et al., 2011). Vitamin D₃ is synthesised in the skin and is present in some food sources (Holick et al., 2011), and is the most common type of vitamin D found in supplemental form in New Zealand. Vitamin D (D₂ or D₃) is not hormonally active, but must undergo two hydroxylations to form the active form of vitamin D, calcitriol, otherwise known as 1,25-(OH)₂D (Holick et al., 2011). The process by which this occurs is now described.

5.1.5. Endogenous synthesis of vitamin D₃

When UVB radiation (wavelengths 290-315nm) reaches unprotected skin and reacts with 7-dehydrocholesterol (7-DHC), the highest concentrations of which are in the basal cell and spinous cell layers of the epidermis (Shahriari et al., 2010), it undergoes a photolytic reaction

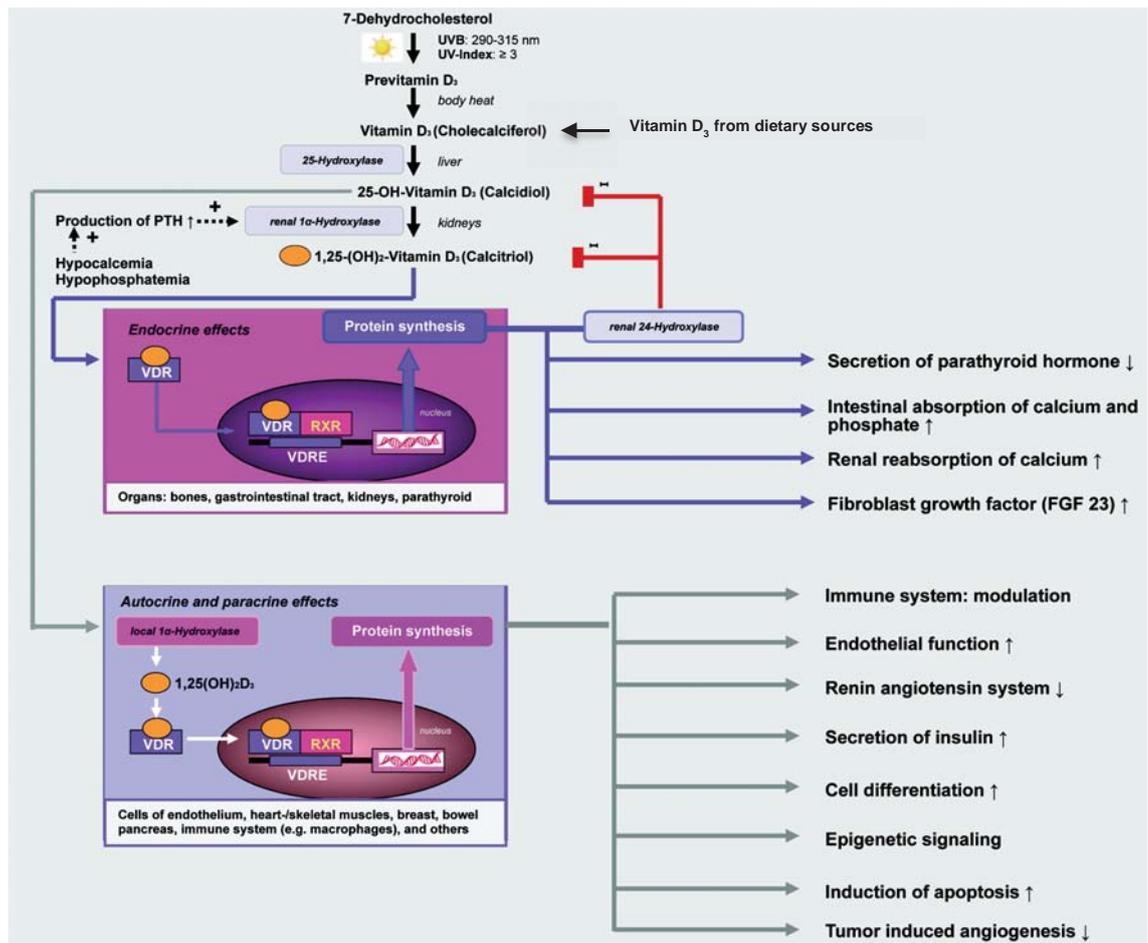


Figure 4. Pathway of vitamin D metabolism¹

Circulating (calcidiol; 25(OH)D) and hormonally active (calcitriol; 1,25(OH)₂D) forms of vitamin D are produced from exposure of skin to UVB light or from vitamin D₃ in the diet. Though binding to the VDR on target cells, active vitamin D regulates the expression of more than 200 different genes, including those related to bone health, cell life (proliferation, differentiation, apoptosis) and the immune system.

¹This adapted figure is based on the article Gröber, Spitz, Reichrath, Kisters, & Holick (2013). Vitamin D: Update 2013: From rickets prophylaxis to general preventative healthcare. *Dermato-Endocrinology*, 5(3), 331-47.

resulting in pre-vitamin D₃, which then slowly undergoes thermal isomerisation to vitamin D₃ over the next four days (Webb, Kline, & Holick, 1988) (Figure 4). Vitamin D₃ is then thought to diffuse from the epidermis into the dermal capillary bed, where it is either stored in adipose tissue or bound to vitamin D binding protein (DBP) and transported to the liver (Holick, 2008c). There, it is converted to 25-hydroxyvitamin D₃ (25(OH)D₃; calcidiol) by vitamin D-25-hydroxylase (25-OHase) in the first of two hydroxylations. Finally, calcidiol is bound to DBP and transported to the kidney and other tissues, where it is hydroxylated to hormonally active

calcitriol by 1α -hydroxylase (1α -OHase) (Lehmann, Querings, & Reichrath, 2004). Vitamin D₂/D₃, calcidiol and calcitriol are all often referred to interchangeably as vitamin D.

The skin has a large capacity to make vitamin D: in a person exposed to a single minimum erythema dosage of sunlight, that is, the minimum amount of time exposed to sunlight so the skin will turn a light pink colour without burning, between 10,000 and 20,000 IU of vitamin D is produced (Heaney, 2008b). The time to achieve a single minimum erythema dose in a light-skinned person wearing minimal clothing in summer is about 15 minutes. Despite the magnitude of these levels, vitamin D intoxication has never been reported as a result of excessive sun exposure (Heaney, 2008b). This is due to feedback mechanisms in the vitamin D pathway that prevent any of the metabolites from reaching potentially toxic levels. Once pre-vitamin D₃ and vitamin D₃ have been formed in the skin, they absorb UVB and UVA radiation and convert them to a wide range of photoproducts that have minimal, if any, effect on calcium metabolism (Holick, 2008c). Calcitriol production in the kidney also has its own feedback mechanisms, with levels of serum phosphate and calcium, fibroblast growth factor, parathyroid hormone and calcitriol itself ensuring concentrations are kept in strict homeostasis (Holick, 2008c).

Calcitriol exerts the majority of its physiological functions genomically, *via* binding to the VDR on the nucleus of target cells (Bikle, 2014). This receptor-ligand complex combines with the nuclear retinoid X receptor (RXR), which in turn recognises and binds to specific DNA sequences called vitamin D response elements, which code for vitamin D-regulated genes. Through this active VDR-RXR-DNA complex, expression of genes specific to that particular DNA sequence is altered. Calcitriol bound to VDR in cell membranes can also produce non-genomic effects that are much more rapid than those involving gene transcription (Bikle, 2014).

5.1.6. Vitamin D levels in New Zealand

Despite the skin's large vitamin D production capacity, low levels of vitamin D are common, both in New Zealand (Mason, Templeton, & Weerasekera, 2012) and worldwide (Whiting,

Green, & Calvo, 2007). The most recent findings in New Zealand, from 2008/2009, showed the annual mean level for adults to be 63 nmol/L (Mason et al., 2012), which is considered vitamin D insufficient according to the Endocrine Society's recommendations (discussed below). Thirty-two percent of New Zealand adults were vitamin D deficient, with levels < 50 nmol/L (Mason et al., 2012).

5.1.7. Factors affecting endogenous synthesis of vitamin D

A number of factors determine the extent to which vitamin D can be endogenously synthesised, including latitude, ozone, season and time of day, as well as age, skin pigmentation, sunscreen use and dress code (Holick, 1995). Other factors, such as obesity, affect the bioavailability of vitamin D (Wortsman, Matsuoka, Chen, Lu, & Holick, 2000).

The influence of latitude, season and time of day on vitamin D production is due to their relationship with the zenith angle of the sun (Holick, 2008a). For UVB light to reach the skin and react with 7-DHC, it must first pass through the ozone layer and enter the atmosphere. As the angle of the sun becomes more oblique to the surface of the earth, which is most pronounced at higher latitudes, in the winter months, and early/late in the day, the photons must travel a longer path through the ozone layer, which effectively absorbs them (Holick, 2008a). It has been estimated that in the wintertime, vitamin D production is severely limited at latitudes north or south of about 35°, as essentially all the UVB is absorbed by ozone (Holick, 2008a). Lifestyle factors associated with winter, such as less time spent outdoors and exposing less skin to the sun, also mean that vitamin D production will be more limited during the winter months.

Endogenous vitamin D production is also reduced in older people and in those with darker skin. From the age of about 20 years, the concentration of 7-DHC in the epidermis begins to decline, restricting the amount of previtamin D that can be formed upon sunlight exposure (Holick, 1995). With regards to skin tone, darker skin contains more melanin, which acts as a natural sunscreen, absorbing more UVB light and thus decreasing the efficiency of vitamin D synthesis (Holick, 2008a). Wearing clothes that do not allow adequate skin exposure, which is of

particular relevance to some cultures and religions, and the proper application of sunscreen, are other factors that will prevent vitamin D formation (Holick, 1995).

5.1.8. Dietary sources of vitamin D

Food sources

Vitamin D can also be obtained through the diet, albeit in small amounts, especially relative to the amount that can be produced through sun exposure. Natural dietary sources predominantly contain the D₃ form, and include oily fish such as salmon and mackerel, and liver oils from cod, tuna and shark (Holick & Chen, 2008). The amount of vitamin D₃ in fish is variable as it depends on the diet of the fish, and therefore farmed fish can have considerably lower amounts than wild-caught fish (Chen et al., 2007). Sundried mushrooms can provide small and variable amounts of vitamin D₂ (Holick, 2008c). The only other notable food sources of vitamin D are those that have been fortified. Vitamin D fortification is voluntary in New Zealand and it can be found added to a selection of margarine and fat spreads, reduced-fat dairy products (e.g., milk, yoghurt), plant-based dairy substitutes (e.g., soy milk) and liquid meal replacements (for examples, see **Table 6**) (Ministry of Health, 2016). There is very limited data on the exact amount of vitamin D found in specific foods in New Zealand. The results of an analysis of several foods conducted at the Institute of Food, Nutrition and Human Health at Massey University, Palmerston North in 2008-2009 (Thomson & Cressey, 2014) are presented in Table 6. Importantly, as there is such a limited number of foods that naturally contain vitamin D, it is nearly impossible to achieve desirable levels of vitamin D solely through dietary sources (Holick, 2008a).

Vitamin D supplements

As dietary sources of vitamin D are so limited, and because there are so many factors that can contribute to reduced endogenous production, consuming vitamin D in supplemental form is a convenient means by which to increase systemic vitamin D levels. Vitamin D supplements are inexpensively available as a single compound, coupled with another vitamin or mineral (e.g.,

Table 6. Vitamin D content of selected foods in New Zealand¹

Food name	Vitamin D content (µg/100g)	Vitamin D content (IU/100g)
Bread, white, sliced, prepacked	0.27	11
Milk, high calcium, 0.1% fat, Meadow Fresh	0.66	26
Butter, spreadable, semi-soft (fortified)	4.45	178
Cottage cheese, light, 1% fat	4.00	160
Yoghurt, Greek style, Fresh 'n' Fruity (fortified)	7.30	292
Egg, chicken, boiled	1.75	70
Egg, whole, raw	1.50	60
Sausage roll, individual size, microwaved	0.29	12
Margarine, poly, 70% fat, reduced salt (fortified)	17.19	688
Margarine, poly, 50% fat, 'Flora Light' (fortified)	16.25	650
Salmon, King, New Zealand, raw	20.14	806

IU, International Unit

¹Source: Thomson & Cressey (2014)

calcium, omega-3) or as part of a multivitamin (**Table 7**). Typical doses range from around 100 to 800 IU in a multivitamin, to 1,000 IU, the most common dose and the maximum amount available in New Zealand without a prescription. A prescription-only dose of 50,000 IU (Cal.D.Forte) is also available for treatment of vitamin D deficiency. In contrast, capsules up to 10,000 IU are available over-the-counter in the United States. Vitamin D₃ is now the preferred form of oral vitamin D; vitamin D₂ supplements used to be commonplace but have declined in popularity, probably reflecting the finding that vitamin D₂ upregulates enzymes that increase degradation of vitamin D₂ and D₃, thereby leading to a faster decline in calcidiol (Heaney, 2008b).

As vitamin D is fat soluble, dosing regimes can be either daily (e.g., 1,000 IU per day) or intermittently (e.g., 50,000 IU per fortnight, 100,000 IU per month) (Kearns et al., 2014). It has been estimated that for every 100 IU of vitamin D ingested, the serum calcidiol concentration increases by 1 ng/ml (2.496 nmol/L) (Heaney, Davies, Chen, Holick, & Barger-Lux, 2003; Holick & Chen, 2008).

Table 7. Examples of vitamin D₃ supplements available in New Zealand.

Brand and name	Vitamin D ₃ / capsule or spray (IU)	Manufacturer's suggested dose
<i>Prescription only</i>		
Cal.D.Forte	50,000	If < 25 nmol/L in serum: loading dose of 1/day for 10 days, then 1/month
	50,000	If 25 – 50 nmol/L in serum, 1/month
<i>Over-the-counter</i>		
Blackmores Vitamin D ₃	1,000	1 daily
Lifestream Vitamin D ₃ Oral Spray	200	5 sprays (1,000 IU)
Nordic Naturals Vitamin D ₃ Oral Drops	1,000	1 daily
Radiance Vitamin D ₃ Chews	1,000	1 daily
Swisse Calcium + Vitamin D	333	2 – 3 daily
Good Health Women's Multivitamin	800	1 daily

IU, International Unit

Oral formulations of calcitriol are also available as prescription-only medicines for use in conditions such as postmenopausal osteoporosis, osteodystrophy or secondary hyperparathyroidism in those with chronic renal failure, and rickets (Medsafe, 2006). However, as oral calcitriol supplementation overrides the otherwise tight regulation of calcitriol concentrations, designed as such to keep calcium and phosphate levels in a state of homeostasis, it can quickly lead to symptoms of vitamin D toxicity, namely hypercalcaemia and hypercalciuria (Medsafe, 2006). Therefore, calcium intake should be minimised, and calcium levels strictly monitored during treatment. In the case of hypercalcaemia symptoms, treatment must be stopped until normocalcaemia ensues (Medsafe, 2006).

5.1.9. Physiological factors affecting response to supplementation and vitamin D status

Once vitamin D obtained through food or supplements has been absorbed through the small intestine and transported by chylomicrons to the liver, it is subject to the same transformations as vitamin D₃ formed in the skin, contributing to serum calcidiol concentration and ultimately

forming hormonally active calcitriol (Holick, 2008c). There are inverse relationships between the magnitude of change in serum calcidiol following supplementation and baseline calcidiol concentration (Mazahery, Stonehouse, & von Hurst, 2014; Zittermann, Ernst, Gummert, & Borgermann, 2014), and between serum calcidiol concentration and BMI/body fat percentage (Didriksen et al., 2013). Those who are obese tend to have significantly lower serum calcidiol than those of healthy weight despite normal epidermal 7-DHC levels and conversion to previtamin D₃ (Wortsman et al., 2000). The prevailing theory is that because vitamin D is a fat-soluble vitamin, the greater amounts of adipose tissue in obese persons means that more vitamin D is sequestered into this tissue from the blood stream (Wortsman et al., 2000).

Other factors are also known to affect vitamin D status, or the availability of vitamin D for physiological use. One group of factors associated with variance in calcidiol concentrations are polymorphisms of the DPB gene. Different phenotypes of DBP, which binds to and transports the majority of calcidiol in serum, predicted different calcidiol concentrations in a multiple regression analysis that accounted for season, sunbathing, smoking and use of vitamin D supplements (Lauridsen et al., 2005). Recently, high levels of CRP, a marker of systemic inflammation, have also been associated with lower calcidiol concentrations, although more information about this relationship has not yet been determined (Ghashut, Talwar, Kinsella, Duncan, & McMillan, 2014).

5.1.10. Definitions of vitamin D status and recommended intakes

Although calcitriol is responsible for the physiological functions of vitamin D, serum levels of calcidiol are considered the best indicator of vitamin D status (Holick et al., 2011; Thacher & Clarke, 2011). Serum calcidiol concentrations normally reflect the amount of vitamin D produced through sun exposure and from stores in adipose tissue, as well as that consumed through the diet (Ross et al., 2011). It also has a reasonably long half-life of two to three weeks (Holick et al., 2011; Thacher & Clarke, 2011). In contrast, calcitriol, in addition to being tightly regulated, is not a good reflection of vitamin D status as it has a short half-life of around four

hours (Holick et al., 2011). In fact, serum concentrations of calcitriol are likely to be normal even in the case of vitamin D deficiency, as low calcium levels due to vitamin D deficiency cause secondary hyperparathyroidism and stimulate its production (Holick et al., 2011). Probably, the only instances in which measurement of calcitriol is relevant are in cases of hereditary disorders of calcidiol or phosphate metabolism (Holick et al., 2011).

The serum concentrations of calcidiol that reflect vitamin D deficiency, sufficiency and optimal levels, and the related recommended levels of intake, are a matter of great controversy and are subject to ongoing debate. This has been made most clear when comparing the reports and recommendations from the Institute of Medicine (IOM) (Ross et al., 2011) and the Endocrine Society (ES) (Holick et al., 2011), which have provided Dietary Reference Intakes (DRIs), and recommendations to prevent and treat vitamin D deficiency, respectively. Common to both sides of the argument is that concentrations of serum calcidiol should be at least 50 nmol/L. Also common is the derivation of this concentration from studies relating calcidiol with bone health outcomes, based on the more robust evidence in this area compared with for other health outcomes. The divergence in recommendations occurs most notably in terms of what constitutes vitamin D sufficiency, or optimal concentrations of calcidiol, and the related recommended daily intake. While the IOM unequivocally states that there is no apparent evidence for benefit of serum concentrations > 50 nmol/L, the ES confidently supports a concentration of at least 75 nmol/L as being vitamin D sufficient, with < 50 nmol/L and 50 – 74 nmol/L representing a state of vitamin D deficiency and insufficiency, respectively. As such, the vitamin D intakes (based on the assumption of minimal sun exposure and/or low initial levels) required to achieve vitamin D sufficiency also differ (see **Table 8**). The IOM recommends a daily intake of 600 IU per day for adults up to the age of 70 years, and 800 IU per day for those > 71 years. In contrast, the ES suggests that while such intakes are the minimum intake required for bone health and muscle function, between 1500 IU and 2000 IU per day may be necessary for people of healthy weight to maintain a concentration of above 75 nmol/L, and that people who are obese (BMI > 30 kg/m²) or on medications affecting vitamin D

metabolism (of which there is a wide range, including anticonvulsants and glucocorticoids) require a dose at least two to three times this (i.e., 3000 – 4000 IU or 4500 – 6000 IU per day) to achieve the same calcidiol concentrations. Furthermore, they suggest that even higher doses of up to 10,000 IU per day are required to treat vitamin D deficiency.

While it does not appear that this debate will be resolved any time soon, there are several key points that should be considered when deciding what serum calcidiol concentration, and thus, intake, to aim for. Firstly, the most favourable outcomes relating to bone health and calcium absorption have been found to occur at serum levels of at least 75 – 80 nmol/L (Heaney, 2013). Across 675 autopsies conducted by Priemel et al. (2010), the fraction of osteoid volume per bone volume (OV/BV) was not at pathologic levels (i.e., $\geq 2\%$ OV/BV, indicating osteomalacia) in any person who had had a calcidiol concentration of at least 75 nmol/L. In contrast, $OV/BV \geq 2\%$ was present in some who had concentrations between 50 – 75 nmol/L. As excess osteoid is a hallmark of vitamin D deficiency, this suggests that calcidiol concentrations < 75 nmol/L are suboptimal (Heaney, 2013). In another study, postmenopausal women ($n = 34$) with an average serum calcidiol level of 50 nmol/L increased their mean levels to > 80 nmol/L and increased the efficiency of intestinal calcium absorption by 45 – 65%. Although this sample was small, a point of strength was that the authors were able to show an increase in calcidiol within the same individuals led to dramatic improvements in calcium absorption (Heaney, Dowell, Hale, & Bendich, 2003). Further to this point, meta-analyses by Bischoff-Ferrari et al. have demonstrated a reduction in fracture risk accompanies calcidiol concentrations ≥ 75 nmol/L (Bischoff-Ferrari et al., 2005).

The second point of consideration is that higher concentrations of calcidiol have also been associated with reduced risk of a wide range of health conditions, such as several cancers (including lung, colon, breast, prostate and lymphoma), falls and lower extremity function, infectious diseases (as reviewed by Heaney, 2008a), autoimmune diseases including type 1 diabetes, multiple sclerosis and Crohn's disease (Kriegel, Manson, & Costenbader, 2011), mental health conditions including depression (Maddock, Berry, Geoffroy, Power, &

Hyppönen, 2013) and dementia (Littlejohns et al., 2014), and cardiovascular diseases (Wang et al., 2012). Increased risk of some cancers, autoimmune diseases, hypertension and schizophrenia has also been observed in those living at higher latitudes, where UVB exposure is reduced, compared to those at lower latitudes (as reviewed by Holick, 2008c).

A third point to consider with regards to optimal vitamin D status is the high concentration of calcidiol that can be reached through normal physiological production when exposed to UVB in sunlight. Populations living under traditional conditions in East Africa, where the human species evolved, have an average calcidiol concentration of 115 nmol/L (Luxwolda et al., 2013). In outdoor workers in temperate climates, calcidiol levels > 200 nmol/L are not uncommon (Barger-Lux & Heaney, 2002; Vieth, 1999). These findings suggest that even 75 nmol/L, as suggested by the ES, could be a conservative estimate of vitamin D sufficiency.

Finally, one should consider what levels have been associated with adverse effects. Signs of acute vitamin D toxicity include hypercalcaemia (serum calcium \geq 2.63 mmol/L) and hypercalciuria (urinary excretion of calcium > 250 mg/day in women or 275 – 300 mg/day in men, or > 0.3 mg of calcium/mg of creatinine) (Ross et al., 2011). Hypercalcaemia and hypercalciuria can cause vascular and soft tissue calcification and nephrolithiasis (kidney stones), respectively, and clinical signs can also include anorexia, weight loss, polyuria, fatigue and heart arrhythmias. Symptoms can occur within four weeks of continual ingestion of excess amounts of vitamin D (Ross et al., 2011). The highest serum calcidiol concentration at which these symptoms can be avoided is unknown, but it is thought that levels probably need to exceed at least 375 nmol/L for them to occur (Holick et al., 2011). While the ES suggests 250 nmol/L as a cautionary Upper Limit (UL) to ensure a safety margin (Holick et al, 2011), the IOM remains even more conservative in its stance, recommending that levels above 125 – 150 nmol/L be avoided due to the unknown consequences of maintaining higher levels over the long-term (Ross et al., 2011). As such, the IOM recommends an UL of 4000 IU per day, stating that “the UL is not a target intake; rather, the risk for harm begins to increase once intakes surpass this level” (Ross et al., 2011, p. 56). Yet, this UL was derived from a starting intake of

10,000 IU per day, which the IOM cedes is probably a safe level of intake. Their recommended UL is based on the assumption that this dose should not raise calcidiol concentrations to above 125 – 150 nmol/L. While the ES also suggests 4000 IU per day as the UL for adults, they propose doses of up to 10,000 IU of vitamin D per day (taken under medical supervision) for the correction of vitamin D deficiency (Holick et al, 2011).

All in all, the picture is a confusing one. There is a great deal of conflicting evidence, and there is no short-term method by which to elucidate the unknowns surrounding long-term higher doses. In the face of the evidence for benefit at serum calcidiol concentrations > 75 nmol/L, the conclusions made by the ES were with the objective of maximising health outcomes weighed up against the potential for risk, and stated that “ample evidence provided the panel with a high level of confidence that toxicity of vitamin D at the recommended doses is quite unlikely” (Holick et al., 2011, p. 1925). Furthermore, it has been suggested that raising serum calcidiol to at least 75 nmol/L provides most tissues and cells in the body with enough substrate to promote local production of calcitriol (Holick, 2008c; Peterlik & Cross, 2006). Thus, in any research investigating the benefit of vitamin D for non-skeletal health outcomes such as for skin and immune health, it seems unlikely that employing the minimum calcidiol concentrations and vitamin D intakes for bone health maintenance will be enough to produce any nutritional benefit of vitamin D. Adopting the ES’s suggestions, then, serum calcidiol should be at least 75 nmol/L, with intakes between 1500 and 2000 IU per day to maintain this dose. As at least a third of the New Zealand population is obese, and another third is overweight (Ng et al., 2014), it could be estimated that a higher intake of at least 3000 – 4000 IU is required to maintain serum levels ≥ 75 nmol/L in the majority of the population.

Table 8. Comparison between the Institute of Medicine and the Endocrine Society definitions of vitamin D status and recommended intakes¹

	Institute of Medicine	Endocrine Society
<i>Vitamin D status (nmol/L)</i>		
Deficiency	< 30	< 50
Insufficiency	30 – 49	50 – 74
Sufficiency	50*	≥ 75
Upper limit of safety	125	250
<i>Recommended intakes (IU/d)</i>		
19 – 70y	600	1,500 – 2,000
≥ 71y	800	1,500 – 2,000
Upper limit**	4,000	10,000

IU, International Unit

*Measures of serum calcidiol levels corresponding to the Recommended Dietary Allowance (RDA) and covering the requirements of at least 97.5% of the population. Based on an assumption of minimal or no sun exposure.

**Defined as the highest daily intake likely to pose no risk.

¹Sources: Holick et al. (2011); Ross (2011)

5.2. Vitamin D and psoriasis

The debate about optimal vitamin D status and what constitutes an adequate dose has only emerged over the past few decades. In the mid-20th century, when the earliest trials investigating the use of oral vitamin D (as D₂) took place, the use of very high doses of vitamin D did not appear to be so controversial, as suggested by the doses used in these trials. Adults and children with chronic and generalised psoriasis were given doses of vitamin D₂ ranging from 25,000 IU per day in children and 50,000 – 100,000 IU per day in adults (Kindler, 1949) to 600,000 IU twice a week in adults (Grandbois, 1955). In the patients involved in Kindler (1949), 12 of 31 patients had total or near-total resolution of lesions within a few weeks or months. A further seven patients also improved, but more slowly, and six did not improve at all. Of note, some who had initially cleared completely had mild relapses within one to three months. Consequent to such large doses of vitamin D, the patients suffered many side effects, including gastric pain and nausea, tiredness, loss of appetite and depression. Thus, while these early studies seemed to suggest some benefit of vitamin D for psoriasis, at least in some people,

results were far from conclusive, and side effects were rife. Probably as a result, interest in this area was to wane until 20 to 30 years later, when exciting new links between vitamin D and psoriasis began to emerge.

5.2.1. Vitamin D and keratinocytes

In the 1970s, it was determined that nearly every cell and tissue in the human body possessed the VDR (Stumpf et al., 1979). At the time, psoriasis was considered a disease primarily of keratinocyte hyperproliferation, and this new evidence showed that keratinocytes responded to vitamin D. In 1988, Smith et al. found that cultured keratinocytes from psoriasis patients had inhibited proliferation and underwent terminal differentiation in a dose-dependent manner when exposed to calcitriol (Smith et al., 1988). Since then, the regulating effects of calcitriol on keratinocyte proliferation and differentiation have been consistently demonstrated (Samuel & Sitrin, 2008). Calcitriol enacts these effects by binding to keratinocyte VDR and triggering transcription of genes that affect proliferation and differentiation (Samuel & Sitrin, 2008). Keratinocyte differentiation is tightly linked to an increase in intracellular free calcium, and calcitriol promotes normal differentiation by stimulating an influx of calcium into the cell (van de Kerkhof, 1995). Calcitriol also stimulates expression of the calcium receptor, making the keratinocyte more able to respond to calcium's pro-differentiating effects (Ratnam, Bikle, & Cho, 1999). The importance of calcitriol for keratinocyte differentiation is illustrated by the abnormal differentiation that occurs in both VDR null (Xie et al., 2002) and 1 α -OHase null mice (Bikle et al., 2004). High levels of calcitriol also promote apoptosis in keratinocytes (Lehmann, 2009), and therefore help to reduce epidermal hyperplasia (Kaštelan et al., 2009).

As well as being able to respond to calcitriol, keratinocytes also have the capacity to produce calcitriol from its initial precursor, 7-DHC (Lehmann, 2009). This involves producing the necessary enzymes to convert vitamin D₃ to calcidiol (25-OHase), and calcidiol to calcitriol (1 α -OHase) (Lehmann, 2009). The amount of calcitriol that is produced is absolutely dependent on the availability of calcidiol (Heaney, 2008a), which suggests two things: that in a state of

vitamin D deficiency, calcitriol production and therefore the actions of vitamin D will be restricted; and also that increasing the amount of available calcidiol from suboptimal levels should promote the production of calcitriol, and therefore its influence on the cell.

5.2.2. Vitamin D and the immune response

When the definition of psoriasis progressed from a disease of keratinocytes to a disease of the immune system, vitamin D did not lose its relevance. While immune cells such as T-cells and dendritic cells do not quite possess the complete vitamin D pathway, they do express the enzyme 1α -OHase as well as the VDR, and can therefore also locally produce calcitriol in the presence of adequate calcidiol and respond to its actions (Baeke et al., 2010).

In psoriatic skin, calcitriol inhibits the proliferation and activation of pro-inflammatory cytokines that promote the Th1 and Th17 pathways, and instead, stimulates T-cells to produce anti-inflammatory Th2 cytokines such as IL-10, leading to a reduced production of cytokines such as IFN- γ and TNF- α (Soleymani, Hung, & Soung, 2015). It also promotes a phenotype in dendritic cells that promotes tolerance to antigens, and the generation of regulatory T-cells, which suppress the immune response (van der Aar et al., 2011), and as mentioned in Chapter 2, appear to have a reduced ability to proliferate in psoriatic skin (Sugiyama et al., 2005). Further, vitamin D is a major regulator of the production of antimicrobial peptides such as cathelicidin by keratinocytes, and as previously stated, cathelicidin has been shown to bind to DNA and thus trigger the development of psoriatic plaques (Dombrowski, Peric, Koglin, Ruzicka, & Schaubert, 2010). In normal skin, vitamin D increases the production of cathelicidin when needed to fight infection, yet it is not yet known specifically how vitamin D influences cathelicidin in psoriasis and contributes to the overall reduction in inflammation seen with the application of topical vitamin D analogues to psoriatic plaques (Dombrowski et al., 2010; Mattozzi, Paolino, Richetta, & Calvieri, 2016).

5.2.3. Psoriasis and vitamin D receptor polymorphisms

Several studies have suggested that polymorphisms of the VDR gene, specifically FokI, BsmI, ApaI, TaqI and A-1012G, are associated with susceptibility to psoriasis (Dayangac-Erden, Karaduman, & Erdem-Yurter, 2007; Kaya et al., 2002; Okita, Ohtsuka, Yamakage, & Yamazaki, 2002; Richetta et al., 2014; Saeki et al., 2002). However, results have been largely conflicting, and a recent meta-analysis of these studies, most of which had notable limitations, found no significant associations between psoriasis and any of the polymorphisms after adjustments for multiple comparisons (Stefanic, Rucevic, & Barisic-Drusko, 2013). One reason that has been proposed for some of the inconsistencies found in relation to the associations between VDR polymorphisms and psoriasis susceptibility is that they might only occur in particular subgroups (Richetta et al., 2014). For instance, recent findings suggested that the FokI polymorphism might be associated with increased risk of severe psoriasis in males with psoriasis, and that ApaI might be associated with increased risk of severe psoriasis in those with psoriatic arthritis (Richetta et al., 2014). The TaqI, FokI and Cdx2 VDR polymorphisms have also been associated with the likelihood of response to topical vitamin D analogues, although findings in this area have been similarly inconsistent (Dayangac-Erden et al., 2007; Zhao et al., 2015), plausibly for similar reasons. Understanding of the potential relationship between VDR polymorphisms and both psoriasis susceptibility and response to vitamin D is therefore still in the preliminary stages, with firm conclusions lacking.

5.2.4. Psoriasis and topical vitamin D and its analogues

A combination of the mechanisms of reduced keratinocyte proliferation, increased keratinocyte differentiation and immunomodulation explain the therapeutic effects of topical vitamin D and its analogues on psoriasis (Shahriari et al., 2010). An early randomised, double-blind, placebo-controlled trial of the calcitriol analogue calcipotriol in 30 patients was pivotal in the acceptance of topical vitamin D analogues as a psoriasis treatment. Moderate to excellent improvement was seen in two of nine on a low dose, five of nine on a moderate dose, and seven of nine on a high dose (Kragballe, Beck, & Sogaard, 1988). The same participants were treated with

placebo on comparable lesions, and only one of 27 people had a moderate improvement. Of importance, no participants had any adverse reactions, and serum calcium levels were not affected. Topical calcipotriol was consequently added to the armament of first-line treatments for mild psoriasis, and the long-suspected association between psoriasis and vitamin D was confirmed.

Like all topical treatments, the ability of topical calcitriol to treat moderate to severe psoriasis is limited by the practicalities of application, and more extensive psoriasis is better suited to systemic treatments. It has been hypothesised that keratinocytes are also able to respond to calcitriol in serum, and further, that they can use calcidiol in serum for the local production of calcitriol (Bikle, 2012; Lehmann, 2009). However, neither of these hypotheses has been confirmed, and in fact, Lehmann (2009) argues against the likelihood of adequate uptake of serum calcidiol by keratinocytes, suggesting that the amount of free calcidiol (i.e., not bound to DPB, approximately 0.03% of total calcidiol) able to enter the cell might be too small to allow sufficient local production. Yet, a number of studies of oral calcitriol in psoriasis (Morimoto et al., 1986; Perez et al., 1996; Smith et al., 1988; Takamoto et al., 1986), alongside those showing associations between serum calcidiol concentrations and psoriasis severity (Bergler-Czop & Brzezińska-Wcisło, 2016; Chandrashekar et al., 2015; Kincse et al., 2015) and a recent pilot study of oral vitamin D₃ in psoriasis (Finamor et al., 2013), all suggest that oral calcitriol/calcidiol may have systemic effects that benefit psoriasis.

5.2.5. Psoriasis and oral calcitriol

Early investigations into the effect of oral calcitriol on psoriasis were conducted by Morimoto et al. (1986). A year prior, Morimoto and Kumahara had reported a chance finding: a woman presenting with psoriasis, rheumatoid arthritis, osteoporosis and vitamin D deficiency had complete clearance of psoriasis plaques following supplementation with oral 1 α -hydroxyvitamin D₃ (1 α -OHD₃), a synthetic precursor to calcitriol (as cited in Morimoto et al., 1986). This case study triggered their subsequent investigations into both topical and oral

calcitriol, and the small flurry of studies that focused on the effect of calcitriol or its analogues on psoriasis over the next decade (Morimoto et al., 1986; Perez et al., 1996; Smith et al., 1988; Takamoto et al., 1986). As with the earlier supplementation of vitamin D₂, some patients taking calcitriol or its analogues experienced dramatic improvements in their skin condition. In the largest trial ($n = 85$), which used calcitriol, 88% had some improvement, 26.5% of which was complete clearance, and 36.2% was moderate improvement (Perez et al., 1996). Similar results were found using 1 α -OHD₃ or calcitriol by Morimoto et al. (1986), Takamoto et al. (1986) and Smith et al. (1988), who had sample sizes of $n = 21$, $n = 7$ and $n = 14$, respectively. Yet, while these results appeared to hold promise, only limited confidence could be placed in them as the trials were small, lacked control groups and used open-label dosing. Including such factors in the trial design was of particular importance, as was the randomisation of participants, as psoriasis did not improve in every participant taking vitamin D, and the reason for this could not be ascertained.

Only one randomised, double-blind, placebo-controlled study assessing the effect of oral calcitriol or its analogues has been conducted. Siddiqui & Al-Khawajah (1990) gave 50 adult males 1 μ g/day of 1 α -OHD₃ or placebo for 12 weeks. Forty-one participants completed the study (equal dropouts per group), and minimal improvement (reduction in PASI score of < 33%) was seen in comparable proportions of the treatment and placebo groups (45% vs. 38%, respectively; difference not significant). Thus, the results of this trial did not support a benefit of oral, active vitamin D analogues for psoriasis. However, at 12 weeks' duration, this trial was much shorter than others that had suggested a benefit of vitamin D for psoriasis. These other trials lasted a minimum of six months, and in many participants, it took longer than one or two months for psoriasis to improve. Furthermore, in some people, psoriasis continued to improve after three months, and even after six months (Takamoto et al., 1986; Smith et al., 1988). Therefore, it could be concluded that the Siddiqui & Al-Khawajah (1990) trial needed to have been at least three months longer for a more robust assessment of the effects of vitamin D against placebo.

Aside from the somewhat larger ($n = 85$) but still open-labeled and uncontrolled study of Perez et al. in 1996, interest in oral vitamin D as a treatment for psoriasis began to diminish once again during the 1990s, with several factors probably contributing to this. Firstly, some oral calcitriol trials showed promising outcomes, but results were not consistent. Secondly, some people appeared to be (hyper)sensitive to the calciotropic effects of oral calcitriol, and while close monitoring of calcium levels, gradual dose increases, bedtime dosing and low-calcium diets helped to alleviate this, it seemed that adverse effects could not be completely avoided. These points are illustrated by a small study ($n = 8$), in which the majority of participants ($n = 6$) had no improvement in psoriasis following oral calcitriol for 6 months, five participants had abnormally high urinary calcium excretion levels (more than 400 mg over 24 hours) and two had decreases in platelet count (el-Azhary, Peters, Pittelkow, Kao, & Muller, 1993). While the regime of bedtime dosing coupled with a low calcium diet appeared more promising in terms of maintaining the normalcy of calcium levels, the requirement for a low calcium diet prohibited its long-term usefulness.

Alongside these concerns with oral active vitamin D, the weight of attention was shifting not only to its topical form, but also to other systemic treatments that were being developed for psoriasis throughout the 1980s and 1990s. Ultraviolet-B and PUVA phototherapy, oral retinoids (acitretin) and ciclosporin were showing relatively good efficacy in treating more widespread psoriasis. In the company of these newly established treatments, oral active vitamin D analogues ceased to be pursued as potential treatments for psoriasis.

5.2.6. Serum calcidiol concentrations in the psoriatic population

As mentioned earlier, keratinocytes and immune cells have the ability to produce calcitriol from calcidiol, with the determining factor being the available concentration of calcidiol. One hypothesis that could be drawn from this is that those with psoriasis have lower levels of calcidiol, and that the correspondingly lower calcitriol production is implicit in the development of psoriasis. From the opposite perspective, perhaps the presence of psoriasis somehow leads to

lower calcidiol levels. A number of studies have investigated whether circulating concentrations of calcidiol are lower in people with psoriasis compared to the wider population, with conflicting results.

Lower levels of serum calcidiol in those with psoriasis compared to controls have been found in at least four observational studies (Bergler-Czop & Brzezińska-Wcisło, 2016; Chandrashekar et al., 2015; Gisoni et al., 2012; Orgaz-Molina, Buendia-Eisman, Arrabal-Polo, Ruiz, & Arias-Santiago, 2012). In a study based in Spain, Orgaz-Molina et al. (2012) observed lower mean serum calcidiol in 43 randomly selected outpatients with psoriasis compared to 43 age- and gender-matched controls (61 ± 19 nmol/L vs. 74 ± 23 nmol/L; $p = 0.007$). Furthermore, 26% of psoriasis patients were vitamin D deficient (< 50 nmol/L), compared with just 9% of controls ($p = 0.04$, OR 2.75 [95% CI 1.02 – 7.96], and 79% of patients were vitamin D insufficient (< 75 nmol/L) compared with 58% of controls ($p = 0.037$, OR 1.36 [95% CI 1.01 – 1.83]). In a multivariate analysis, the authors showed a strong association between the presence of psoriasis and vitamin D insufficiency after adjusting for BMI, age, gender, dietary vitamin D intake, total sun exposure and Fitzpatrick skin phototype (OR 2.89 [95% CI 1.02 – 7.64], $p < 0.03$).

Similar findings were made by Chandrashekar et al. (2015), Bergler-Czop et al. (2016) and Gisoni et al. (2011), whose case-control studies each showed significantly lower serum calcidiol levels in patients with psoriasis than in healthy controls. In a study based in India, Chandrashekar et al. (2015) compared calcidiol in 43 people with psoriasis with 43 age- and gender-matched controls, and found the mean serum calcidiol of cases to be 33 ± 17 nmol/L, compared to 56 ± 46 nmol/L in controls ($p = 0.004$). The findings of Bergler-Czop et al. (2016), in Poland, showed very similar serum calcidiol concentrations to Chandrashekar et al. (2015) in their cases (32 ± 7 nmol/L, $n = 40$) and controls (56 ± 7 nmol/L, $n = 40$), also with a significant difference between them ($p = 0.048$). In Gisoni et al. (2011), based in Spain, mean calcidiol in those with psoriasis ($n = 145$) was 52 ± 28 nmol/L versus 93 ± 31 nmol/L in controls ($n = 141$, $p < 0.01$). Vitamin D deficiency (< 50 nmol/L) was present in 57% of psoriatic patients compared to 30% of controls ($p < 0.001$). In their multiple regression

analysis, vitamin D deficiency was again associated with the presence of psoriasis (OR 2.5 [95% CI 1.18 – 4.89], $p < 0.01$) independently of age, gender, BMI, calcium levels, parathyroid levels and season of blood sampling.

Importantly, the group of interest in each of these studies consisted of people whose psoriasis was moderate-to-severe. Mean PASI score in Chandrashekar et al. (2015) was 15.2 ± 8.6 , and in Bergler-Czop et al. (2016) it was 10.4 ± 6.3 , which are considered severe and moderate psoriasis, respectively. In Gisoni et al. (2011), mean PASI was 7.1 ± 10 , i.e., moderate psoriasis, and while mean PASI was only 4.4 (SD not given) in Orgaz-Molina et al. (2012), mean body surface area (BSA) was also 4.4 (SD not given), which is considered moderate psoriasis. It could be speculated that these participants spent less time outdoors than controls, yet neither Chandrashekar et al. (2015) nor Orgaz-Molina et al. (2012) found any differences in the estimated hours of sunlight per week between groups ($p = 0.60$ and $p = 0.84$, respectively). While these observational studies can only demonstrate association, and not causation, the results do suggest a relationship between the presence of moderate-to-severe psoriasis and lower levels of serum calcidiol.

In contrast, analysis of data from the 2003 – 2006 National Health and Nutrition Examination Survey in the United States showed no difference between the calcidiol levels of those with psoriasis (60 [95% CI 57 – 64] nmol/L, $n = 148$) when compared to the general population (59 [95% CI 57 – 61] nmol/L, $n = 5,693$, $p = 0.37$) (Wilson, 2013). Thirty-three percent of those with psoriasis and 35% of controls were vitamin D deficient (< 50 nmol/L, $p = 0.67$), and 72.5% of those with psoriasis and 76% of controls were insufficient (< 75 nmol/L, $p = 0.29$). When age, gender, ethnicity, season and BMI were accounted for, those with psoriasis had a non-significant 0.65 nmol/L greater calcidiol level ($p = 0.71$). Yet, these results do not contradict those of the case-control studies described above for two main reasons. Firstly, the psoriatic sample in Wilson (2013) consisted mostly of those with mild or very mild psoriasis (< 1 hand palm coverage, $n = 81$; 1 – 2 hand palms, $n = 40$; 3 – 10 hand palms, $n = 20$; > 10 hand palms, $n = 7$), whereas the other three studies only included those with at least moderate BSA.

Another recent small study found no difference in calcidiol between 20 people with very mild psoriasis (median PASI 2.4 ± 3.6) and 20 controls (52 ± 17 nmol/L vs. 63 ± 7 nmol/L, $p = 0.73$) (Zuchi, Azevedo, Tanaka, Schmitt, & Martins, 2015). Therefore, it is possible that serum calcidiol concentrations in those with mild psoriasis are comparable with those in the general population, but are lower in those with more severe psoriasis. This is supported by the second point, which is that Wilson (2013) found a trend towards lower calcidiol in those with BSA > 10 palms compared to those with minimal BSA (-12 nmol/L, $p = 0.07$), with the small number of people with BSA > 10 palms the clear limiting factor in this analysis.

A recent case-control study involving 50 patients in Iran who did have severe psoriasis (mean PASI score 12.15 ± 11.76 [$> 12 =$ severe psoriasis]) also found similar calcidiol concentrations in these patients compared to healthy controls (37 ± 16 nmol/L vs. 31 ± 11 nmol/L, $p = 0.06$) (Maleki, Nahidi, Azizahari, Meibodi, & Hadianfar, 2016). However, these results demonstrate the high rate of vitamin D deficiency in both groups: 84% of cases had calcidiol concentrations < 50 nmol/L compared to 93% of controls ($p = 0.21$). Therefore, the possibility that low levels of vitamin D in the cases contributed to psoriasis cannot be excluded.

The question addressed by the above studies is whether low vitamin D levels are related to the presence of psoriasis. Based on these results, it is not possible to say conclusively whether those with psoriasis have lower serum calcidiol concentrations than the wider population. However, the outcomes of several studies suggest this could be the case for those with moderate to severe psoriasis.

5.2.7. Associations between serum calcidiol concentrations and psoriasis severity

The next question is whether there is a relationship between calcidiol concentration and psoriasis severity, and attempts to determine this have also produced conflicting results.

Observational studies

The results of at least three cross-sectional studies have shown significant inverse associations

between serum calcidiol concentration and psoriasis severity. Those with moderate to severe psoriasis (determined by use of systemic treatments; $n = 34$) had significantly lower calcidiol concentrations than those with mild psoriasis (determined by use of topical treatments; $n = 7$) at all quartiles of calcidiol: Q1 = 32 vs. 45 nmol/L; median = 51 vs. 61 nmol/L; Q3 = 75 vs. 84 nmol/L; $p < 0.05$ for all (Kincse et al., 2015). Analysis of the 43 cases in Chandrashekar et al. (2015) also showed a strong negative correlation between calcidiol concentration and PASI ($r = -0.71$; $P \leq 0.001$), as did analysis of the 40 cases in Bergler-Czop et al. (2016) ($r = -0.43$; significance not given).

If an inverse relationship between serum calcidiol and psoriasis severity were to be confirmed, it would support the proposal that raising serum calcidiol might improve psoriasis. Increasing serum calcidiol concentration can be done easily and safely through vitamin D₃ supplementation or UVB exposure, which contrasts to the challenges around increasing calcitriol with its accompanying effects on calcium levels. Higher serum calcidiol could hypothetically provide keratinocytes and immune cells with enough substrate to increase local production of calcitriol, while having no impact on the homeostatic mechanisms regulating systemic calcitriol concentrations. Continuing the hypothesis, this locally-produced calcitriol would then enact its known effects on keratinocyte proliferation and differentiation and on the immune response.

However, neither Gisoni et al. (2011) nor Orgaz-Molina et al. (2012) found a significant correlation between calcidiol and PASI score. Yet, these null results could have stemmed from the limitations of correlation analysis, which cannot account for confounding factors, which is important as a wide range of factors affects psoriasis severity. Adjusting for such factors can make it possible to see relationships that might otherwise be obscured. The analyses used in these studies were also limited to identifying a linear relationship, yet it is possible that calcidiol and psoriasis severity are related in a non-linear fashion. These points are also relevant when considering the lack of correlations seen in phototherapy trials, as described below.

UVB-phototherapy intervention studies

Vitamin D is formed in the skin upon exposure to UVB light, that is, at the same wavelengths that are effective in treating psoriasis (290 – 315nm) (Osmancevic et al., 2010). Studies of the efficacy of UVB phototherapy in psoriasis demonstrate improved (i.e., lowered) PASI scores alongside simultaneous elevation of serum calcidiol levels (Osmancevic et al., 2009a; Osmancevic et al., 2009b; Romani et al., 2012; Ryan et al., 2010; Vahavihu et al., 2010). A significant negative correlation between PASI and calcidiol was seen in one study (strength of relationship not given; $p = 0.047$), in which mean calcidiol increased from 90 ± 35 nmol/L to 155 ± 47 nmol/L ($p < 0.001$) and mean PASI improved from 9.2 ± 4.9 to 2.7 ± 1.6 ($p < 0.001$) (Osmancevic et al., 2009a). However, no relationship between calcidiol and PASI was observed in four similar studies, in which serum calcidiol levels increased by between 27 nmol/L and 60 nmol/L and PASI scores improved by between 55% and 93% (Osmancevic et al., 2009b; Perez et al., 1996; Romani et al., 2012; Vahavihu et al., 2010). These findings are perhaps to be expected when considering that UVB therapy induces a number of other beneficial responses in skin that are unrelated to vitamin D (Schwarz, Navid, Sparwasser, Clausen, & Schwarz, 2012).

5.2.8. Psoriasis and oral vitamin D

At the time of writing this review, aside from the early 20th century studies using vitamin D₂, just one very small study had used oral vitamin D₃ with the intent to raise serum calcidiol and assess any subsequent effect on psoriasis severity. In an open-label pilot study, Finamor et al. (2013) gave 9 men and women with psoriasis 35,000 IU of vitamin D₃ a day for 6 months. As this was a large dose of vitamin D, participants excluded milk, dairy products and calcium-fortified products from their diet and consumed a minimum of 2.5 L of fluid per day to avoid excessive calcium absorption and concentrated urinary calcium, respectively. Over the treatment period, mean serum calcidiol concentration increased from 37 ± 18 nmol/L to 265 ± 80 nmol/L ($p < 0.0001$) and PASI scores significantly improved in all nine patients ($p = 0.0023$). There was a significant inverse relationship between PASI score and calcidiol level (r

= -0.56, $p = 0.001$), and linear regression analysis further supported this association ($r^2 = 0.32$; $p = 0.015$). While it is not possible to draw any firm conclusions from these results due to the lack of control group, they strongly support further investigation into whether raising serum calcidiol through oral vitamin D₃ supplementation improves psoriasis.

5.2.9. Summary and conclusion

Several attempts have been made over a number of decades to demonstrate whether a relationship exists between serum calcidiol and psoriasis, and whether oral vitamin D (both oral calcitriol and just recently, vitamin D₃) is beneficial for psoriasis. Overall, these have yielded inconclusive results, yet the factors that link vitamin D and psoriasis at a pathophysiological level, considered alongside the associations between lower serum calcidiol and more severe psoriasis in cross-sectional and case-control studies, as well as the promising results from the recent pilot study suggest that further investigation is warranted. In light of this evidence, and alongside findings of the previous chapters which emphasise the difficulties arising from the limitations of available treatments for psoriasis, there is strong support for the notion that a randomised controlled trial using vitamin D₃ to safely raise serum calcidiol concentrations without affecting calcium levels, and involving a control group for comparison, is an important avenue of exploration. The remainder of this chapter describes the implementation and findings of a trial that aimed to identify whether oral vitamin D₃ is an effective treatment for psoriasis, based on the hypothesis that taking a monthly supplement of 100,000 IU of vitamin D₃ over 12 months (200,000 IU at baseline) will significantly reduce PASI score compared to taking an identical placebo. The following section provides the methodological detail of how this trial was conducted.

5.3. Methods

5.3.1. Recruitment and screening

Participants were recruited between April 2012 and March 2013 *via* information provided to medical centers and Auckland-based dermatologists (Appendix 7); articles in local newspapers (media releases in Appendix 8); email to a database of people interested in research at the university's Nutrition Department (Appendix 9); and advertisements placed online (social media, the University website and a research website). One hundred and sixty-nine people enquired about taking part and were assessed for eligibility. People were eligible to take part in this study if they were aged 18 years or older and had chronic plaque psoriasis. They were excluded if they had chronic kidney or liver disease, were smokers, took ≥ 1000 IU vitamin D supplements per day or had taken them within the last 2 months, were pregnant or breastfeeding or planning to become pregnant in the next year, or were undergoing UVB phototherapy. Where supplemental vitamin D < 1000 IU/day was regularly taken at the time of enrolment, continuation was permitted since changes in serum calcidiol concentration with lower doses of vitamin D would be minimal compared to changes following a baseline dose of 200,000 IU; it was also only permitted when taken as part of a multivitamin. Otherwise, participants were asked not to take other supplements containing vitamin D during the trial period. Due to the length of the trial, existing psoriasis treatments were permitted upon enrolment if they had been used for more than 3 months immediately prior to the start of the trial. For ethical reasons and because it would likely result in significant attrition, participants were not prohibited from starting new treatments during the trial period, but they were asked to only do so if it was absolutely necessary, and to closely document when they began using the treatment and how often so these could be accounted for in analysis.

Potential participants were provided with an information sheet providing details of the study (Appendix 10) and completed an online screening questionnaire (Appendix 11), and those who met the criteria underwent baseline measurements including a skin assessment. Sixty-eight people were excluded from taking part: 44 for not meeting eligibility criteria, 19 declined to

participate, and 5 for other reasons (e.g., fear of needles). Enrolment in the study was completed once the study's dermatologist (based off-site) had viewed photographs of each participant's skin and confirmed the presence of psoriasis. In the case of uncertain diagnosis, a consultation was arranged between that person and the dermatologist for confirmation of psoriasis. Examples of email communication with participants in relation to recruitment and enrolment in the study are included as Appendix 12. One hundred and one participants were eligible, provided consent and were randomised onto treatment ($n = 67$) or placebo ($n = 34$). Over the course of the study, four participants in the treatment group and one in the placebo group discontinued the intervention or were lost to follow-up (**Figure 5**). Further details of the randomisation process and study procedures are described below.

5.3.2. Study design

This research was conducted as a single-centre, randomised (with a 2:1 ratio), double-blind, placebo-controlled, parallel-group trial. Due to the length of the trial and the accessibility of vitamin D supplements, a 2:1 ratio of treatment:placebo was chosen with the aim of enhancing recruitment, as it gave people more than a 50/50 chance of receiving the treatment (Pocock, Clayton, & Stone, 2015). In order to group participants according to psoriasis severity, 38 blocks of three randomly ordered treatment allocations (1, 2 and 3) were computer-generated. A third party, a trained pharmacist who was not otherwise involved in this research, designated two numbers as treatment (vitamin D) groups and one number as the placebo group, and allocated the capsules into identical bottles. Bottled capsules were stored in boxes labeled 1, 2 or 3 until allocated to participants. All participants and researchers on the study remained blinded to which number related to each treatment until the trial had concluded and serum calcidiol concentrations had been analysed.

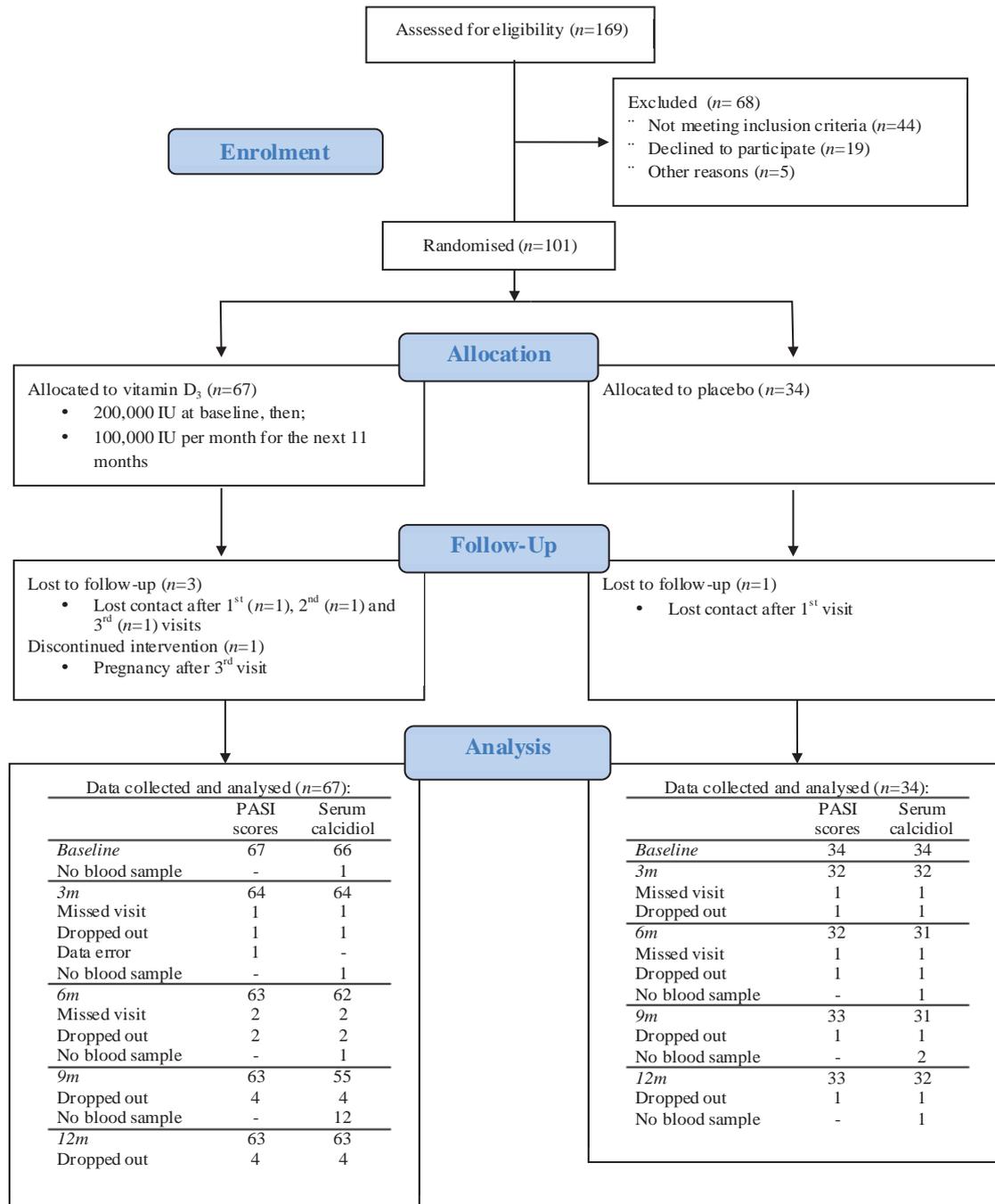


Figure 5. Flow diagram of participant numbers through different phases of the study.

PASI, Psoriasis Area and Severity Index

5.3.3. Ethics and trial registration

This study was approved by the Health and Disability Ethics Committee (NTX/11/07/063/AM01) (Appendix 13). Approval from the Standing Committee on Therapeutic Trials (SCOTT) was also required to allow the distribution of vitamin D as a mega-dose (Appendix 14). All participants provided informed, signed consent before undergoing any assessments (Appendix 15). The trial was also registered with the Australian New Zealand Clinical Trial Registry, #12611000648921, prior to its commencement.

5.3.4. Study procedures

Participants attended appointments every three months (i.e., seasonally) for a total of five visits over a one-year period. Seasonal assessments of vitamin D and psoriasis allowed natural variations in both of these factors to be accounted for, by ensuring each participant had one measurement per season. Initial (baseline) appointments for the first participants took place in June 2012, and the final appointments were in March 2014. Of the treatment group, 15 began the trial in spring, 32 in summer and 20 in winter. In the placebo group, 6 began in spring, 14 in summer, 2 in autumn and 12 in winter. All appointments were conducted at Massey University's Human Nutrition Unit in Auckland, New Zealand (latitude 37°S). Details of each visit are given below.

Initial (baseline) study visit

The first visit involved collection of participants' personal details, assessment of their psoriasis severity and other psoriasis characteristics, demographics, skin phototype and anthropometrics. Participants also underwent blood sampling to enable the analysis of serum calcidiol concentrations, calcium and albumin and high-sensitivity C-reactive protein (hsCRP). Further details of these assessments are provided below.

The first visit was particularly important due to the need to establish a good rapport with participants and to help them feel that their participation was worthwhile, especially given that they would be required to attend a further four visits. Participants were scheduled to attend

their appointments at times that were convenient for them, which sometimes meant early in the morning, after office hours, or on the weekend. To manage the safety issues around this, there were at least two researchers or staff present in the Nutrition Research Unit at any time. Participants were greeted promptly and professionally, and efforts were made to help them feel comfortable and relaxed.

There were four main stages to each participant visit. For baseline visits, these were conducted as follows:

- *Stage One: Welcome, completion of forms and height measurement*

Participants were welcomed in the main room of the Nutrition Unit and thanked for taking part in the study. The aims of the study and what it involved were reiterated, based on the information sheet that they had previously received. Participants were then given the opportunity to ask any questions, and reminded that they could do so at any time. They were asked to complete a form that gave their formal consent to participate in the study (Appendix 15), as well as to complete forms that covered basic personal (Appendix 16) and demographic details (Appendix 17): participant ethnicity, country of birth and (where relevant) time in New Zealand, type of residential area (e.g., urban, rural), level of education, employment type and status, and relationship status.

Once a participant had completed these forms, their height was measured twice using a stadiometer following a standardised method.

- *Stage Two: Psoriasis characteristics and history, weight and body fat, and assessment of psoriasis severity*

This part of the visit involved a shift from the main room of the Nutrition Unit to one of the private consultation rooms. The participant was asked about their psoriasis-related characteristics and medical history, in line with the questions in Appendix 18. They were asked about their age when psoriasis first developed, whether there was a known family history, whether they usually experienced marked seasonal changes (e.g., a worsening in winter; if so

they were deemed a “summer responder”), current treatments (including dosage if applicable, frequency of use and start date) and presence of psoriatic arthritis. Also noted was the use of any medications that could exacerbate psoriasis (beta blockers, lithium, systemic steroids, interferon, antimalarials, tetracyclines or NSAIDs) (Basavaraj, Ashok, Rashmi, & Praveen, 2010), and presence of any other health conditions.

Participants’ skin type was classified according to the Fitzpatrick scale, which ranges from Type I (pale white skin, blond or red hair, blue eyes, freckles, always burns/never tans) to Type VI (deeply pigmented dark brown to darkest brown skin, never burns/ never tans) (Sachdeva, 2009). This was done by taking skin colour into account alongside asking participants about their propensity towards burning/tanning.

Participants’ body weight and body fat percentage were then assessed using bioelectrical impedance analysis (BIA) (InBody 230, Biospace Co. Ltd., Seoul) and following a standardised procedure. To measure body fat percentage with this model of BIA, a person stands on a base that has two metal footpads similar to weighing scales, and holds onto a pair of handles that also have metal pads attached to them. Over a short time (~a minute), the BIA provides a measure of ‘electrical impedance’, otherwise described as the degree of opposition to the flow of a very mild electric current through body tissues, and this is then used to estimate body fat percentage (von Hurst et al., 2015). This procedure is quick, safe, relatively accurate (von Hurst et al., 2015) and causes no discomfort to participants other than perhaps from having to stand still.

The next part of this stage of the appointment was the assessment of a participant’s psoriasis. This was done using the PASI, which takes into account both the extent of body surface area affected by psoriasis and the severity of the lesions. PASI is the ‘gold standard’ in clinical trials and the most widely used tool for assessing psoriasis severity (Schmitt & Wozel, 2005). Prior to the commencement of the trial, PASI assessment training had been undertaken in a clinical setting with the study’s consultant dermatologist, to ensure researcher competency in using PASI to assess psoriasis severity.

Participants were tactfully asked if they were happy to undress to their underwear for their psoriasis to be assessed, and they were given the option of wearing a robe and exposing different areas of skin bit-by-bit if they preferred. Assessment of psoriasis severity involved systematically grading the severity of affected skin according to each of three domains – erythema (redness), induration (thickness) and scaling – on a scale from 0 to 4, with scores referring to none, mild, moderate, severe and very severe involvement, respectively. The scoring sheet used for this assessment is included as Appendix 19. The assessment was conducted in the following order: hands (palms, back of hands), arms (front and back), front of torso, front of legs and tops of feet, back, back of legs including buttocks, soles of feet, scalp. A visual reference was used to ensure consistency when choosing grades (Appendix 20). Also recorded was the estimated size of the affected area on each the four regions of the body: the head and neck, the upper extremities, the trunk (including axillae and groin), and lower extremities (including buttocks). The area covered was determined by counting the number of palm-sizes (i.e., the approximate size of the participant’s hand) affected by psoriasis. Photographs were taken of affected areas to send to the study’s dermatologist for confirmation of psoriasis (and thus eligibility to take part in the study). It was also intended that photographs would provide visual references if any clinically meaningful changes in psoriasis were to occur.

- *Stage Three: Phlebotomy (blood sampling)*

Following their psoriasis assessment, participants were accompanied into the phlebotomy room to provide a blood sample. Participants did not have to be in a fasted state for this test. The sample was collected by a qualified phlebotomist using a sterile Vacutainer Flashback Precisionglyde needle and needle holder. Every effort was made to ensure participants were as comfortable as possible during this procedure, for example, they had the option of sitting or lying down if they preferred.

- *Stage Four: Wrap up*

In this final stage of the appointment, participants were accompanied back to the main room of the Nutrition Unit. The next stages of the study were explained to them in detail, in particular the distribution of capsules and when they should take them, and the scheduling of the next appointment. This was all also detailed in a letter for them to take away, included as Appendix 21. Participants were asked if they had any questions, and were given a \$20 petrol voucher to cover transport costs to the University.

- *Post-appointment*

- Blood processing and storage*

In the laboratory, serum was collected for calcidiol, hsCRP, calcium and albumin. All samples were frozen in separate aliquots in small non-reactive tubes and stored at -80°C until analysis (see below).

- Confirmation of psoriasis and assignment of study ID number*

A participant's eligibility to take part in the study was confirmed once the dermatologist had viewed photographs of their skin and the presence of psoriasis established (see email communication in Appendix 12). In the case of an uncertain diagnosis, a face-to-face appointment was arranged between the participant and the dermatologist for further assessment (Appendix 12). Those who were not considered eligible at this point were sent an email advising them of this and the reasons why they were not eligible (Appendix 12), with suggested actions from the dermatologist if necessary (e.g., to seek medical care if they had a different skin condition that required treatment). Once enrolment had been confirmed, participants were assigned a unique ID number, e.g., 2200001. The format of these numbers is as follows: study ID (i.e., 22), length of time on the study at visit (i.e., 00 = baseline, 03 = 3 months, 06 = 6 months....), participant ID (e.g., 001). Participant ID numbers with the relevant month indication were used for all study documents and electronic files to protect participants' privacy.

Calculation of PASI score / Randomisation according to psoriasis severity

Following confirmation of enrolment, data collected during the psoriasis assessment was entered into an online PASI calculation tool (PASI Training, 2008), which then generated an overall PASI score ranging from 0 (no psoriasis) to 72 (very severe). The PASI system itself does not define what is considered mild, moderate or severe psoriasis, but the definition proposed by Schmitt & Wozel (2005) is widely applied, that is, PASI < 7 is considered mild, 7 to 12 is moderate, and > 12 is severe psoriasis. Based on their calculated PASI score, participants in this study were classified according to these definitions of psoriasis severity.

Each participant was then randomised following their first appointment. Participants were grouped according to their psoriasis severity (mild, moderate or severe), then assigned to the next available randomisation table slot in a block of three, grouped according to severity, which corresponded to group 1, 2 or 3. As this was a blinded study, no one directly involved with the study knew which of these numbers corresponded to vitamin D or placebo.

Distribution of capsules and assessment of compliance

Following randomisation, the first three months' capsules were couriered to participants, and they were to receive subsequent capsules at each appointment. These were accompanied by a letter outlining the protocol for taking the capsules. A copy of the letter and the capsule labeling are included as Appendix 22 and Appendix 23, respectively. Participants were asked to take two capsules at baseline, followed by one capsule on the same day each month for the next 11 months.

Participants were sent a text message reminder (or email/phone call if preferred) to take their capsule on the same day each month. They then confirmed they had taken the capsule by reply text/email/phone. If a reply was not received, they were followed up with until there was confirmation. Taking the capsule within one week on either side of their designated day was considered compliant. Confirmation of compliance was recorded in an Excel spreadsheet.

Follow-up visits (visits 2 – 5)

Visits 2 – 5 tended to be shorter than the first visit as they involved fewer assessments, but were conducted in a similar manner overall. When participants arrived, they were welcomed into the consultation room, and following general chat, were asked how their psoriasis was. Participants were asked to describe any changes to psoriasis treatment or non-psoriasis medication, such as stopping or starting a treatment, changing a treatment dosage or using a treatment more or less frequently. Frequency of topical treatment use was then calculated on a weekly basis for each participant. They were also asked whether they had had any major deviations from their normal levels of sun exposure (particularly a holiday to a sunny destination) to help interpret potential changes in serum calcidiol concentrations. The guide for these questions is in Appendix 24. This discussion was followed by an assessment of their psoriasis, a blood test and then the wrap up, in which participants were supplied with their next three months' worth of capsules and a petrol voucher. At their final visit, participants completed an exit questionnaire, primarily to assess their experience of taking the capsules (i.e., any adverse effects or benefits) (Appendix 25). They were also given a letter thanking them for taking part, and explaining when they would be provided with the results of the study (Appendix 26).

5.3.5. Vitamin D₃ and placebo capsules

Supplemental vitamin D₃ was in the form of a mega-dose (cholecalciferol 2.5 mg or 100,000 IU) taken as gelatine capsules. This dose equates to an average intake of 3340 IU per day, which is in the range (1800 – 4000 IU) shown to be required to bring the majority of people to a serum calcidiol concentration of 75 – 110 nmol/L (Ilahi et al., 2008). This dose has been shown to pose no risks of hypercalcaemia or hypercalciuria and is much lower than the generally accepted upper limit of 10,000 IU per day (Heaney, 2008b). The placebo capsule was identical in appearance and composition, but contained no vitamin D₃. Vitamin D₃ and placebo capsules were supplied by Tishcon Corporation (New York, USA). The certificate of analysis for both the vitamin D and the placebo capsules are included as Appendix 27.

5.3.6. Analysis of blood samples

An accredited laboratory was used to carry out the analysis of blood samples (North Shore Hospital Laboratory, Auckland, New Zealand).

Serum from blood collected at each visit (baseline, 3, 6, 9 and 12 months) was analysed to determine calcidiol concentration. This was measured using an automated immunoassay (ADVIA Centaur Vitamin D Total Assay, Siemens Healthcare Diagnostics Inc. [NY, USA]), which has an assay range of 9.2 nmol/L to 374 nmol/L and a coefficient of variation (CV) of 4.8% – 11.1%. Samples for calcidiol only were analysed in one batch after the study had finished to ensure the researchers remained blinded to randomisation. In order to classify participants according to vitamin D status in this study for descriptive purposes, deficiency was defined as a serum calcidiol concentration of < 50 nmol/L, insufficiency as 50 to 74 nmol/L and sufficiency as ≥ 75 nmol/L (Holick, 2008c).

Serum from baseline, 6 and 12 months was analysed for hsCRP concentration, due to the potential of systemic inflammation to confound vitamin D status (Ghashut et al., 2014). This was measured with the Dimension Vista System CardioPhase method (Siemens Healthcare Diagnostics Inc., NY, USA). This has an automatic analytical measurement range of 0.16 – 9.50 mg/L, but samples with results > 9.50 mg/L can be repeated on a higher dilution. It has a CV of 4.0% – 5.4%. Average hsCRP concentration was defined as 1.0 – 3.0 mg/L based on the range provided by the laboratory.

As vitamin D is involved in calcium absorption (Heaney, 2005), serum levels of calcium were also assessed at baseline (as reference), 3 and 12 months to monitor for hypercalcaemia. Serum albumin was also assessed at these time points to allow for adjustment of calcium concentrations, given that a significant proportion (~40%) of total calcium is bound to albumin and is thus biologically inactive (Bushinsky & Monk, 1998). Serum calcium and albumin were measured with the Dimension Vista System; the CA method and ALB method were used for

calcium and albumin, respectively. Normal serum calcium concentration was based on adjusted values and defined as 2.1 – 2.6 mmol/L (Bushinsky & Monk, 1998).

5.3.7. Data handling and statistical analysis

Study data was initially entered into Microsoft Excel spreadsheets under participants' unique ID numbers, then exported into SPSS Statistics v20.0. All statistical analyses were conducted using SPSS.

Power calculations

Power calculations were conducted using Glimmpse (Glimmpse 2.0.0), and were based on detecting an effect of treatment on PASI over five visits. Due to a lack of oral vitamin D₃ trials for psoriasis, the estimated initial mean \pm SD of PASI (9 ± 3) was based on previously successful UVB phototherapy treatments in which significant increases in serum calcidiol concentration were achieved (Osmancevic et al., 2009a; Vahavihu et al., 2010). A 50% reduction in PASI was considered a clinically meaningful improvement in psoriasis (Carlin, Feldman, Krueger, Menter, & Krueger, 2004). Taking the 2:1 randomisation into account and assuming a gradual improvement in PASI over 12 months in the treatment group, a means scale factor of 0.5 and a variability factor of 2, it was calculated that a sample size of 99 in total would be required to detect an effect of treatment, with statistical power equal to 80% and an α -level of 0.05.

Analysis of baseline characteristics

Analyses were conducted on all available data from all participants. Data are presented as mean \pm SD for normally distributed variables and median [25th, 75th percentiles] for non-normally distributed variables. Where possible, non-normally distributed data was transformed using the natural log and is presented as geometric mean [95% CI]. Differences in continuous data between groups at baseline were determined using the Independent T-test for normally distributed data and the Mann Whitney test for non-normally distributed data. Baseline PASI

scores were compared according to season of trial commencement using the Kruskal-Wallis test.

PASI scores

The primary outcome, the effect of vitamin D₃ supplementation on PASI over the five time points compared to placebo, was assessed using a linear mixed model (i.e., a linear model that includes both fixed and random variables). Linear mixed models allow multiple repeated measures for each person to be included and can handle missing values in the data set, which are common in repeated measures trials such as this one, by not excluding cases when some values are missing (Field, 2009). PASI score was the dependent variable, treatment group (vitamin D / placebo), time (baseline, 3 months, 6 months, 9 months and 12 months) and the interaction between treatment group and time (treatment*time) were entered as 'fixed factors', and hsCRP and body fat were entered as covariates (and therefore controlled for) due to baseline differences between groups. A comparable proportion of people in each group started a new treatment during the study (25% of the treatment group and 24% of the placebo group), therefore this was not included in the model. A random intercept was specified for each participant, which controlled for the variability in baseline PASI score between participants, as well as correlated scores over repeated measurements within participants. The fit of the model was assessed by plotting residuals against predicted values to evaluate for normality and homogeneity of variance of residuals (**Figure 6**). These plots showed non-homogeneity of variance, therefore PASI scores were transformed using the natural log following the addition of a constant (0.9) so that the minimum value was one (Osborne, 2010).

A linear mixed model was also used to assess within-group changes in PASI score over time, using time as a fixed factor and a random intercept. Also calculated was the percentage of each group achieving a reduction in baseline PASI score of at least 50% by 12 months.

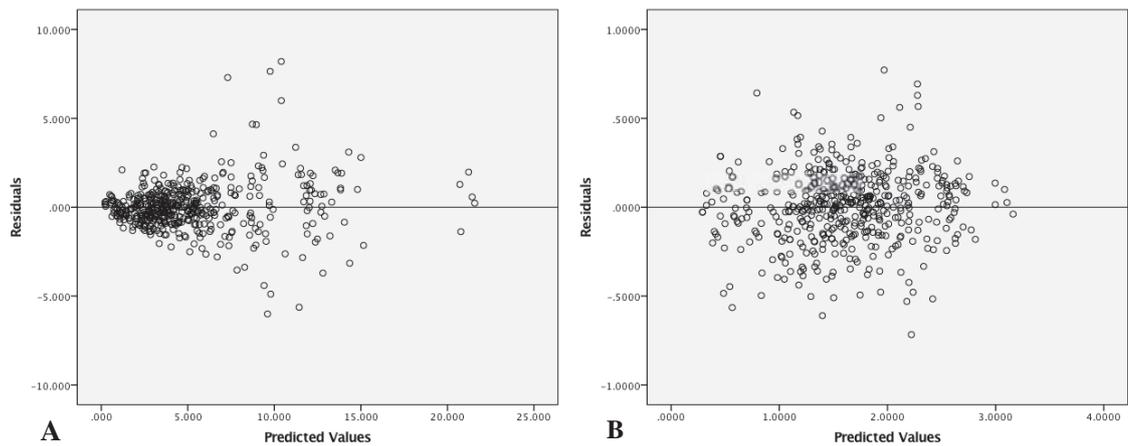


Figure 6. Predicted vs. residual plots for the primary outcome model before and after PASI was log-transformed. Plot (A) shows non-homogeneity of variance of residuals around the reference line compared to relative homogeneity in Plot (B).

Serum calcidiol concentrations

To assess the impact of vitamin D₃ supplementation on serum calcidiol concentrations, differences in serum calcidiol between groups over time were also assessed using a linear mixed model. Treatment group (vitamin D / placebo), time and the interaction treatment group*time were entered as ‘fixed factors’, and body fat percentage was controlled for as a covariate due to its known influence on change in serum calcidiol concentration following vitamin D supplementation (Didriksen et al., 2013). A random intercept was entered for each participant, as above, to account for individual differences in baseline calcidiol concentrations. Residual versus predicted plots showed normal distribution and homogeneity of variance.

Relationship between PASI score and serum calcidiol concentration

To identify whether there was a relationship between serum calcidiol concentration and PASI score over time across the whole sample, a cross-sectional analysis was conducted using a linear mixed model. Ln (PASI + 0.9) was the dependent variable, and a range of potential confounding factors, effect modifiers and individual effects were controlled for to identify the independent relationship between serum calcidiol concentration and PASI score. Continuous covariates were body fat percentage (baseline and 12 months, with interpolated values for 3, 6

and 9 months), hsCRP level (baseline, 6 and 12 months, with 6 and 12 months values carried backwards to 3 and 9 months, respectively), frequency of topical treatments per week, age of diagnosis and Fitzpatrick skin type. Categorical or binary (yes/no) variables were season, gender, known family history of psoriasis, “summer responder”, diagnosed psoriatic arthritis, started new topical treatment in past 3 months, on systemic or biologic psoriasis treatment, on beta-blockers, on systemic steroids (not including psoriasis treatments), on antimalarials, on NSAIDs, and on tetracyclines; these were entered as ‘fixed factors’. Multicollinearity was assessed by visual inspection of a correlation matrix between each predictor. Included for exploratory purposes were two-way interactions between calcidiol concentration and body fat percentage, gender, age of diagnosis, “summer responder”, known family history of psoriasis, Fitzpatrick skin type and diagnosed psoriatic arthritis. Variables with the largest p -values > 0.05 were removed from the model one at a time until all remaining variables were considered significant contributors to the variance in PASI score. Residual plots for the final model showed a normal distribution and improved homogeneity of variance compared to models where PASI had not been log-transformed or had a constant added, reflecting the importance of these transformations for analysing the data (**Figure 7**).

Because of the transformation in PASI scores as described above, the beta-coefficients derived from the model could not be directly interpreted in a meaningful way. Instead, the beta-coefficients were used to calculate estimated average improvements in PASI scores at different increases in calcidiol, in order to determine the hypothetical improvement in PASI following an increase in serum calcidiol concentration based on the fitted model. As serum calcidiol was inversely correlated with body fat percentage, estimated improvements in PASI scores were calculated based on increasing serum calcidiol at increments up to the highest concentration reached by participants according to body fat category.

Firstly, to calculate these estimates, the maximum increase in calcidiol that was observed within each body fat category was determined. Then, the difference between baseline calcidiol and the maximum calcidiol in that category was calculated (“Change required for max”). “Change

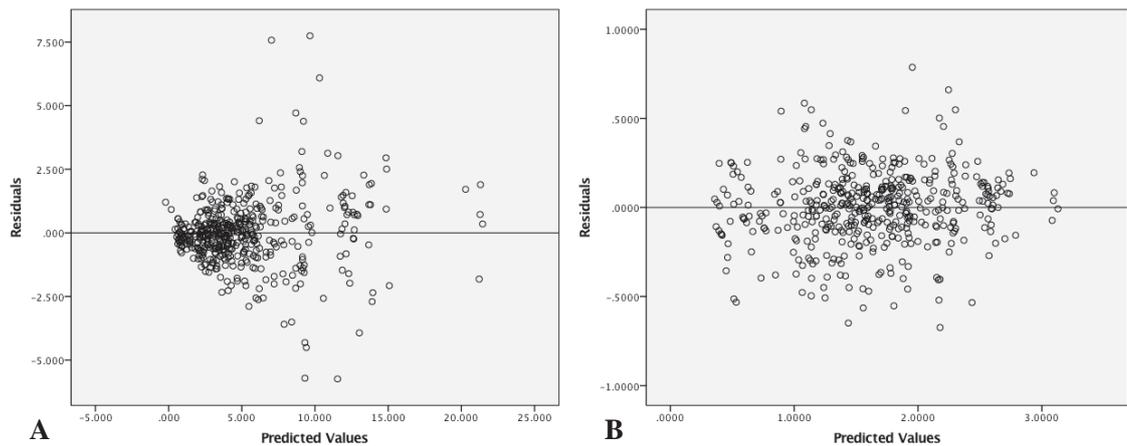


Figure 7. Predicted vs. residual plots for the model assessing the relationship between PASI and serum calcidiol concentration before and after PASI was log-transformed. Plot (A) shows non-homogeneity of variance of residuals around the reference line compared to relative homogeneity in Plot (B).

required for max” was then multiplied by the beta-coefficient for calcidiol (-0.001228). This was then added to the baseline PASI score predicted for each person based on the model. Predicted PASI at maximum calcidiol concentration was calculated by taking the anti-log minus 0.9 of this value. Finally, the predicted PASI at baseline was subtracted from the predicted PASI at maximum calcidiol concentration, with the difference being the improvement in PASI if the maximum calcidiol in that body fat category was achieved. This process was repeated with different values of change in calcidiol to estimate the average improvement in PASI based on these increases. In the results table (Table 15 in Chapter 6), the ‘initial PASI scores’ are those predicted by the model at baseline, and the ranges were chosen based on psoriasis severity (mild 0.1 – 6.9; moderate 7 – 12; severe > 12) (Schmitt & Wozel, 2005). The mild category was further divided as it is a wide range.

The direction of the relationship between PASI and serum calcidiol concentrations for individual participants was also assessed using Pearson’s correlations.

All reported *P*-values were based on 2-tailed tests, and $p < 0.05$ was considered statistically significant.

5.3.8. Communication of results to participants

Approximately eight months after the study ended, participants were emailed a personalised letter advising them of their individual results and the overall study results. An example of this letter is included as Appendix 28.

5.3.9. Funding

The majority of this study was funded by a grant from Lottery Health Commission, and the remainder was funded by Massey University.

This thesis now turns to the findings of this research and a discussion of these findings within the context of the wider literature.

6. Study Two: Findings and Discussion

This chapter presents the second set of original findings in this thesis; those that relate to the aim of determining whether vitamin D₃ supplements are an effective treatment option for plaque psoriasis. It begins with a presentation of the findings, followed by a discussion of these findings within the context of the wider literature.

6.1. Findings

6.1.1. Participant characteristics

Participant characteristics at baseline are presented in **Table 9**. The groups were similar in PASI score, serum calcidiol concentration, age, number of years with psoriasis, family history of psoriasis, weight, BMI and education level. The placebo group had a significantly higher mean serum hsCRP level ($t(98) = 2.231, p = 0.028$; Independent T-test), and there was also a trend towards higher body fat percentage in this group ($t(99) = 1.91, p = 0.058$; Independent T-test). A higher percentage of the placebo group was deficient (< 50 nmol/L) or insufficient (50 to 74 nmol/L) in vitamin D at baseline compared to the treatment group (88% vs. 70%, respectively). The majority of the placebo group (85%) was in employment, while this percentage was lower in the treatment group (76%). The balance of ethnicities between groups was similar except for Pacific and Asian, where there was a higher percentage in the placebo group. There was no difference in baseline PASI between participants who began the trial in different seasons ($H(3) = 0.608, P = 0.90$; Kruskal-Wallis test).

6.1.1. Psoriasis severity (PASI scores)

PASI scores are reported in **Table 10**. The linear mixed model showed that PASI did not differ between groups over the five time points (treatment group $F(1, 106.4) = 0.589, p = 0.44$, treatment group*time $F(4, 370.3) = 0.516, p = 0.72$), indicating that there was no significant difference in psoriasis severity between those on vitamin D₃ and those on placebo when adjusting for differences in hsCRP, body fat percentage and individual variation. This lack of

Table 9. Participant characteristics at baseline by group

	Vitamin D ¹ (n = 67)	%, (SD) or [25 th , 75 th]	Placebo ¹ (n = 34)	%, (SD) or [25 th , 75 th]
Gender (male)	39	58%	17	50%
Age (years)	50.7	(13.4)	46.7	(13.7)
Age of diagnosis (years)	28.0	[16.0, 40.0]	24.5	[15.8, 40.0]
Years with psoriasis	18.0	[10.0, 31.0]	14.0	[6.0, 30.3]
Ethnicity ²	(n = 66)			
NZ European	55	82%	26	77%
Maori or Pacific	4	6%	4	12%
Asian	1	1.5%	3	8.8%
European	4	6.0%	3	8.8%
Other	4	6.0%	0	0%
Weight (kg)	81.3	[77.7 – 85.1]	83.0	[76.2 – 90.3]
BMI (kg/m ²)	27.3	[26.2 – 28.5]	28.7	[26.9 – 30.6]
Body fat (%)	31.7 ^a	(8.8)	35.2	(8.2)
PASI score	5.2	[3.3, 6.5]	4.2	[3.1, 7.0]
Serum calcidiol (nmol/L)	(n = 66) 62	(26)	55	(19)
Vitamin D status:	(n = 66)			
Very deficient (< 25 nmol/L)	3	5%	2	6%
Deficient (25-49 nmol/L)	18	27%	12	35%
Insufficient (50-74 nmol/L)	25	38%	16	47%
Sufficient (75-250 nmol/L)	20	30%	4	12%
hsCRP (mg/L)	(n = 66) 1.21 ^b	[0.94 – 1.57]	2.01	[1.37 – 2.93]
Fitzpatrick skin type:				
I	1	2%	1	3%
II	12	18%	4	12%
III	27	40%	17	50%
IV	22	33%	10	29%
V	5	7.5%	2	6%
Known family history psoriasis (y)	29	43%	15	44%
Residential area:	(n = 66)			
Urban	8	12%	3	9%
Suburban	47	70%	28	82%
Rural	11	16%	3	9%
Highest qualification:	(n = 66)			
None	5	8%	1	3%
Secondary school	15	22%	10	29%
Trade/technical	10	15%	5	15%
Diploma/Bachelors	24	36%	11	33%
Postgraduate	7	11%	5	15%
Professional	5	8%	2	6%
Work status:				
Employed	51	76%	29	85%
Unemployed (not retired)	2	3.0%	0	0%
At-home parent/student	5	7.5%	2	5.9%
Retired	9	13.4%	3	8.8%

NZ, New Zealand; BMI, body mass index; PASI, Psoriasis Area and Severity Index; hsCRP, high sensitivity C-reactive protein

¹Data are number (%), mean (SD), median [25th, 75th percentile], except weight, BMI and hsCRP, which are geometric mean [95% CI]

²7 participants identified as two ethnicities; “Other” includes American, Australian, British, and South African

^a*p* = 0.058 for trend towards difference between groups, Independent T-test

^bSignificantly different to placebo, *p* = 0.028, Independent T-test

difference is further shown by the comparable proportion of people in the vitamin D group (11.9%) and placebo group (11.8%) who achieved a 50% reduction in PASI (i.e., significant clinical improvement) by 12 months (**Table 11**). Furthermore, both the treatment and placebo group had statistically significant improvements in psoriasis severity (i.e., PASI score) throughout the study period. Compared to baseline, analysis using a linear mixed model showed a trend toward a significant difference in the vitamin D group at 6 months ($p = 0.06$), and that PASI score was significantly lower than baseline at 9 months ($p = 0.021$) and 12 months ($p = 0.022$) (Table 10). In the placebo group, PASI had significantly improved from baseline at 6 months ($p = 0.035$), 9 months ($p = 0.019$) and 12 months ($p = 0.001$) (Table 10).

6.1.2. Systemic vitamin D (serum calcidiol) concentrations

Prior to supplementation, the mean serum calcidiol concentrations were similar between the treatment group and the placebo group ($t(98) = -1.502$, $p = 0.14$; Independent T-test) (Table 9). In terms of vitamin D status, more people in the placebo group (41%) than in the treatment group (32%) were considered vitamin D deficient (< 50 nmol/L) at baseline, while more of the treatment group (30%) were vitamin D sufficient (≥ 75 nmol/L) than in the placebo group (12%) (Table 9). Psoriasis severity did not differ between those who were vitamin D deficient (median PASI 5.5 [25th, 75th percentile 3.4, 7.0], $n = 35$), insufficient (median PASI 4.0 [3.0, 6.4], $n = 41$) or sufficient (median PASI 4.6 [3.2, 7.1], $n = 25$) at baseline ($p = 0.42$; Kruskal-Wallis test).

As expected following supplementation, the treatment group had a significantly higher calcidiol concentration than the placebo group from 3 to 12 months ($p < 0.001$ for comparison at 3 and 6 months, and $p = 0.002$ for comparison at 9 months) (**Table 12**). In the treatment group, mean calcidiol increased from 62 nmol/L to 96 nmol/L by 3 months (mean difference 33 [95% CI 27 – 38] nmol/L; $p < 0.001$), reaching a plateau around 103 nmol/L from 6 months onwards (**Figure 8**). Seventy-nine percent of the treatment group had achieved vitamin D sufficiency (≥ 75 nmol/L) by 3 months, and this reached 87% by 9 months (**Table 13**). The remainder of

participants in that group achieved calcidiol concentrations > 50 nmol/L, except for 3 people who became deficient again at 12 months. The maximum serum calcidiol concentration reached with vitamin D₃ supplementation was 194 nmol/L, and this was reached at 12 months after baseline, although this same person had reached 163 nmol/L by 3 months.

In the placebo group, calcidiol concentration increased significantly between 3 and 6 months to 78 nmol/L ($p < 0.001$), which was a mean increase of 24 [95% CI 17 – 30] nmol/L from baseline. The reason for this increase is not clear. It was not a seasonal effect, as most 6 month visits took place in winter or summer (41.2% or 32.4% of the placebo group, respectively), and mean 6 month serum calcidiol concentration in people measured in winter (85 ± 15 nmol/L) was higher than in those measured in summer (78 ± 18 nmol/L). Several participants for whom serum calcidiol increased at this time reported an increase in sun exposure compared to normal; conversely, some reported no change or less sun exposure than normal. Mean serum calcidiol concentrations in the placebo group remained similarly elevated at 9 and 12 months (Figure 8, Table 12). In contrast to the first 3 months, 62% of the placebo group was vitamin D sufficient by 6 months.

Table 10. PASI scores over 12 months by group

	Vitamin D				Placebo					
	<i>n</i>	Unadjusted PASI score ¹	25 th , 75 th percentile	Min, Max	Adjusted PASI score ^{2,a}	<i>n</i>	Unadjusted PASI score ¹	25 th , 75 th percentile	Min, Max	Adjusted PASI score ^{2,a}
0m	67	5.2	3.3, 6.5	0.4, 21.8	4.8	34	4.2	3.1, 7.0	0.8, 13.2	4.5
3m	64	4.7	2.9, 6.8	0.1, 22.0	4.5	32	3.6	2.7, 7.0	0.6, 15.8	4.1
6m	63	4.6	2.6, 7.0	0.2, 23.2	4.4 ^b	32	3.4	1.9, 7.9	0.5, 18.6	3.9 ^c
9m	63	4.0	2.2, 5.9	0.4, 22.0	4.0 ^d	33	3.6	1.9, 6.5	0.4, 16.4	3.8 ^c
12m	63	3.7	2.0, 6.4	0.1, 19.4	3.9 ^d	33	3.4	2.4, 4.9	0.3, 14.6	3.5 ^e

PASI, Psoriasis Area and Severity Index

¹Values are median

²Values are average predicted PASI scores for an individual with mean high-sensitivity C-reactive protein level and body fat percentage as calculated using a linear mixed model with a random intercept per person; values are back-transformed from $\ln(\text{PASI}+0.9)$

^aNo difference in PASI scores between groups over time (treatment group $F(1, 106) = 0.589, p = 0.44$; treatment group*time $F(4, 370) = 0.516, p = 0.72$) as calculated by the linear mixed model adjusted for hsCRP, body fat and a random intercept per person

^bTrend towards significant difference to baseline, $p = 0.06$

^cSignificantly different to baseline, $p < 0.05$

^dSignificantly different to baseline, $p < 0.001$

^eSignificantly different to baseline, $p = 0.001$

Table 11. Percentage of participants achieving $\geq 50\%$ improvement in PASI from baseline

	Vitamin D (<i>n</i> = 67) % (<i>n</i>)	Placebo (<i>n</i> = 34) % (<i>n</i>)
3m	6.0 (4)	0 (0)
6m	7.5 (5)	20.1 (7)
9m	9.0 (6)	14.7 (5)
12m	11.9 (8)	11.7 (4)

PASI, Psoriasis Area and Severity Index

Table 12. Serum calcidiol concentrations over 12 months by group

	Vitamin D				Placebo				<i>P</i> -value ³
	<i>n</i>	Serum calcidiol (nmol/L) ¹	Min, Max	Adjusted serum calcidiol (nmol/L) ²	<i>n</i>	Serum calcidiol (nmol/L) ¹	Min, Max	Adjusted serum calcidiol (nmol/L) ²	
0m	66	62 ± 26	12, 137	61	34	55 ± 19	23, 108	57	0.358
3m	64	96 ± 26	50, 163	94 ^a	32	59 ± 16	29, 93	61	<0.001
6m	62	103 ± 29	51, 180	101 ^a	31	78 ± 16	48, 113	81 ^a	<0.001
9m	55	103 ± 25	54, 180	102 ^a	31	82 ± 22	40, 129	84 ^a	0.002
12m	63	101 ± 29	46, 194	100 ^a	32	80 ± 16	52, 114	83 ^a	0.002

¹Values are mean ± standard deviation.

²Values are predicted calcidiol concentrations for an individual with the mean body fat percentage at each time point, calculated using a linear mixed model at separate time points with body fat percentage as a covariate.

³The overall model showed a significant difference between groups over time (treatment group $F(1, 102) = 18.9, p < 0.001$; treatment group*time $F(4, 372) = 11.4, p < 0.001$), calculated using a linear mixed model with body fat percentage as a covariate and a random intercept per person. Differences between groups at each time point were estimated using a linear mixed model fit separately for each time point, with body fat percentage as a covariate.

^aSignificantly different to baseline, $p < 0.001$, calculated using a different linear mixed model than described in footnote 3, fit separately for each group over time with body fat percentage as a covariate and a random intercept per person.

Table 13. Percentage of participants in each group according to vitamin D status¹

	Treatment (<i>n</i> = 67)			Placebo (<i>n</i> = 34)		
	%			%		
	< 50 nmol/L	50 – 74 nmol/L	≥ 75 nmol/L	< 50 nmol/L	50 – 74 nmol/L	≥ 75 nmol/L
0m	31	37	30	41	47	12
3m	0	21	79	26	47	26
6m	0	16	84	3	35	62
9m	0	13	87	3	38	59
12m	4	9	87	0	32	68

¹< 50 nmol/L, deficiency; 50 – 74 nmol/L, insufficiency; ≥ 75 nmol/L, sufficiency (Holick et al., 2011).

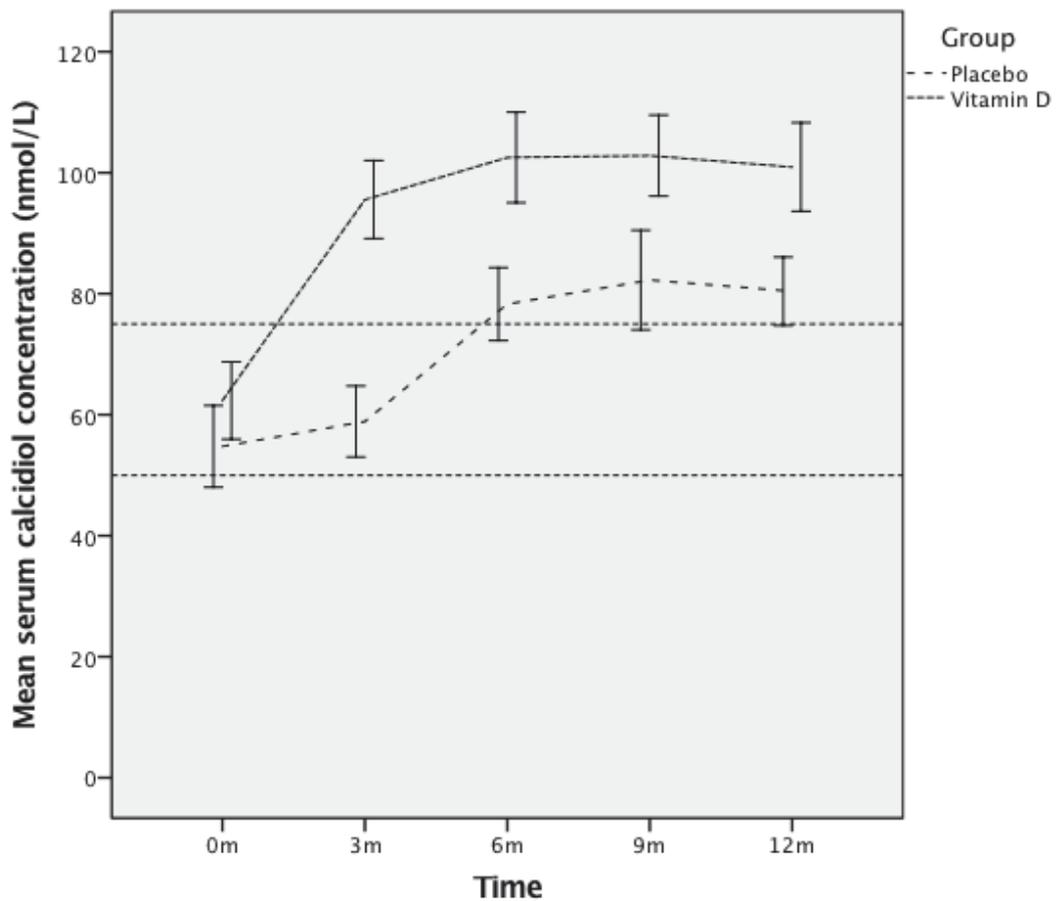


Figure 8. Mean serum calcidiol concentrations over 12 months in each group

Error bars represent 95% confidence intervals. Reference lines are at 75 nmol/L (vitamin D sufficiency) and 50 nmol/L (below which is vitamin D deficiency) (Holick et al., 2011).

6.1.3. Relationship between psoriasis severity and systemic vitamin D

As mentioned in the Methods section of the previous chapter, because of the unexpected elevation of serum calcidiol concentrations in the placebo group, it was decided it would be useful to determine whether there was a relationship between systemic vitamin D levels and psoriasis severity in the group overall. When the PASI scores and calcidiol concentrations of the whole sample were considered together, there was a significant inverse association between serum calcidiol and PASI ($F(1, 409) = 9.517, p = 0.002$) after adjusting for gender, body fat percentage, starting a new topical treatment in the past 3 months and individual differences (i.e., the variation in psoriasis severity that naturally occurs between people; see below). This inverse relationship is shown by plotting partial residuals (residual + fitted coefficient $[-0.002] \times$ calcidiol concentration) against calcidiol concentration and fitting a regression line, as in **Figure 9**.

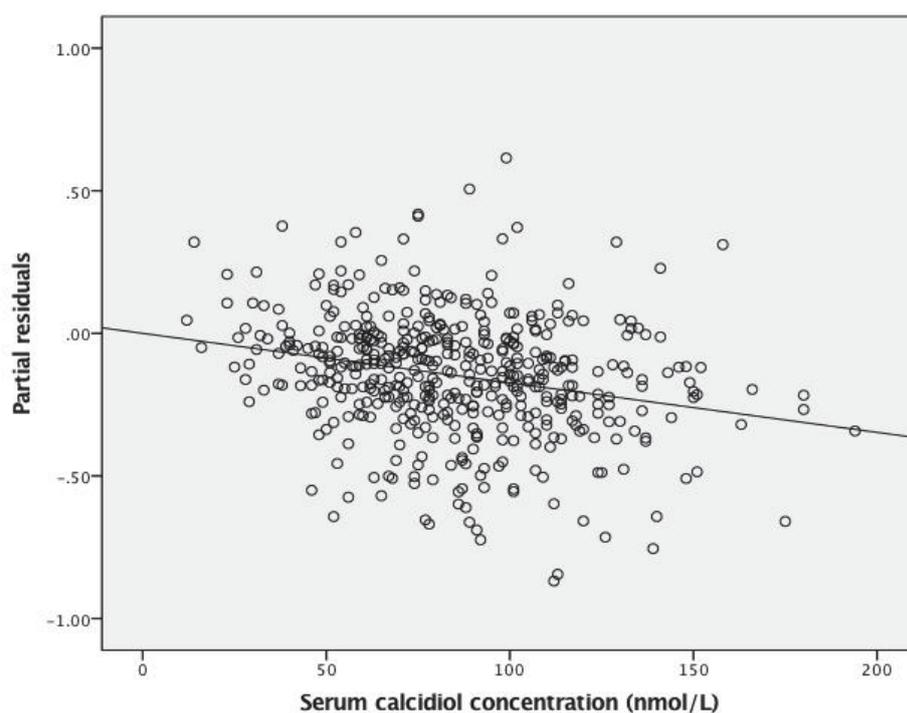


Figure 9. Partial residual plot¹ showing the association of serum calcidiol concentration with PASI score while controlling for gender, body fat, use of new topical treatments in the previous 3 months and individual effects (469 time-points from 101 participants during the 12 month follow-up period).

PASI, Psoriasis Area and Severity Index

¹A partial residual plot shows the relationship between one predictor variable (in this case, serum calcidiol concentration) and the dependent variable (PASI) while controlling for the effects of other predictor variables.

The individual differences in the model refer to the variability in psoriasis severity at baseline (intercepts), and as baseline PASI scores were significantly different across participants (SD of intercepts [range of transformed PASI scores]=0.5 [0.4 – 3.1], $\chi^2(1) = 485.761$, $p < 0.01$), this variability was adjusted for in the analysis. However, there was no variance in slopes ($\chi^2(1) = 0.079$, $p > 0.05$), meaning that there was no significant difference in the way participants' PASI scores related to serum calcidiol concentrations over time.

Beta-coefficients for the transformed data are presented in **Table 14**. Normally, beta-coefficients can be used to interpret the predicted magnitude of change in the dependent variable (i.e., PASI score) based on changes in the variables in the model (i.e., changes in serum calcidiol concentration, body fat, starting a new topical or being male or female). However, due to the data transformations, these coefficients could not be interpreted in the usual manner so instead, they were used to calculate estimated average improvements in PASI from baseline based on different serum calcidiol concentrations (**Table 15**).

Table 14. Linear mixed model beta-coefficients and 95% confidence intervals for variables associated with log-transformed PASI score¹

	β	<i>SE</i> β	95% CI	<i>P</i> -value
Intercept	.752	.243	.274 – 1.23	0.002
Serum calcidiol	-.002	.0006	-.003 – -.0006	0.002
Body fat %	.016	.006	.004 – .027	0.007
New topical in past 3m	.169	.050	.071 – .266	0.001
Gender (male)	.640	.109	.425 – 1.23	<0.001

PASI, Psoriasis Area and Severity Index

¹ $n=101$; dependent variable is $\ln \text{PASI} + 0.9$

The estimated predicted values suggest that elevation of serum calcidiol concentrations by amounts from 25 nmol/L to 125 nmol/L was associated with mild decreases in PASI (range of decrease 0 – 2.6 PASI). Table 15 gives the estimated improvements from baseline PASI at different increments between these concentrations. The degree of improvement differed according to the initial PASI score, and the range of improvement at each increment of serum calcidiol reflects the variability in baseline PASI across the sample. Due to the apparent non-

linear relationship between PASI and serum calcidiol, the estimated average improvement in PASI was greater for those with higher baseline scores. According to the PASI scores at different calcidiol concentrations as estimated with the linear mixed model, there was no threshold effect above which serum calcidiol appeared to have a greater impact on PASI score; in this model, the more that serum calcidiol concentrations increased, the greater the estimated average improvement in PASI.

Visual inspection of the data suggested that not every participant who increased their serum calcidiol concentration improved their PASI score. To investigate this further, correlations between serum calcidiol and transformed PASI score were explored for individuals who had more than two measurements of each ($n = 97$) (**Figure 10**). Rather than the plot being centred on zero, which would be expected if there were no relationship between vitamin D and psoriasis severity, it showed variability in the correlations, with 61 of 97 people (63%) demonstrating an inverse relationship. The range of the correlation was from -0.98 to 1 , and the distribution of correlations was similar between the treatment and placebo groups.

6.1.4. Compliance

Participants' reported compliance with taking the vitamin D₃ supplements as required was very high, with 96.3% of monthly capsules taken within two weeks of their designated day. Of the treatment group, two participants missed two months' capsules (7 – 8 months) (temporarily lost contact with the research team), one participant lost his capsules during the eighth month and took a replacement two weeks after his designated day, and another participant took his 12 month capsule one month late. The effect of the missed capsules on serum calcidiol concentration, if any, is not clear from the data. One participant in the placebo group also lost contact and missed four months' capsules (from 4 – 7 months), and another did not take their 12 month capsule. All of these participants were included in data analysis based on the intention-to-treat principle.

Table 15. Estimated decreases in PASI scores at increments of change in serum calcidiol concentration¹

Initial PASI score ²	Increase in serum calcidiol concentration (nmol/L)				
	25	50	75	100	125
0.6 – 3.4 (<i>n</i> = 34)	0 – 0.1	0.1 – 0.3	0.1 – 0.4 (<i>n</i> = 24)	0.2 – 0.5 (<i>n</i> = 12)	0.3 – 0.6 (<i>n</i> = 5)
3.6 – 6.9 (<i>n</i> = 39)	0.1 – 0.2	0.3 – 0.5 (<i>n</i> = 35)	0.4 – 0.7 (<i>n</i> = 30)	0.5 – 0.9 (<i>n</i> = 17)	0.6 – 0.9 (<i>n</i> = 8)
7.1 – 11.5 (<i>n</i> = 17)	0.2 – 0.4	0.5 – 0.7 (<i>n</i> = 15)	0.7 – 1.0 (<i>n</i> = 11)	0.9 – 1.3 (<i>n</i> = 5)	1.1 – 1.6 (<i>n</i> = 2)
12.0 – 22.3 (<i>n</i> = 9)	0.4 – 0.7 (<i>n</i> = 8)	0.8 – 1.4 (<i>n</i> = 8)	1.2 – 2.0 (<i>n</i> = 6)	1.6 – 2.1 (<i>n</i> = 4)	2.6 (<i>n</i> = 1)

PASI, Psoriasis Area and Severity Index

¹As serum calcidiol was inversely correlated with body fat percentage, the highest change in serum calcidiol levels used to predict PASI for each person was the maximum observed increase in calcidiol achieved by a participant in the same body fat category as that person. *N* for each increment of calcidiol refers to the number of participants in the same body fat category as the participant who achieved the largest increase in serum calcidiol.

²Initial PASI scores are those predicted by the linear mixed model at baseline; ranges are based on psoriasis severity: 0.1 – 6.9 = mild; 7 – 12 = moderate; < 12 = severe (Schmitt & Wozel, 2005). ‘Mild’ was split to further differentiate between low and high mild scores.

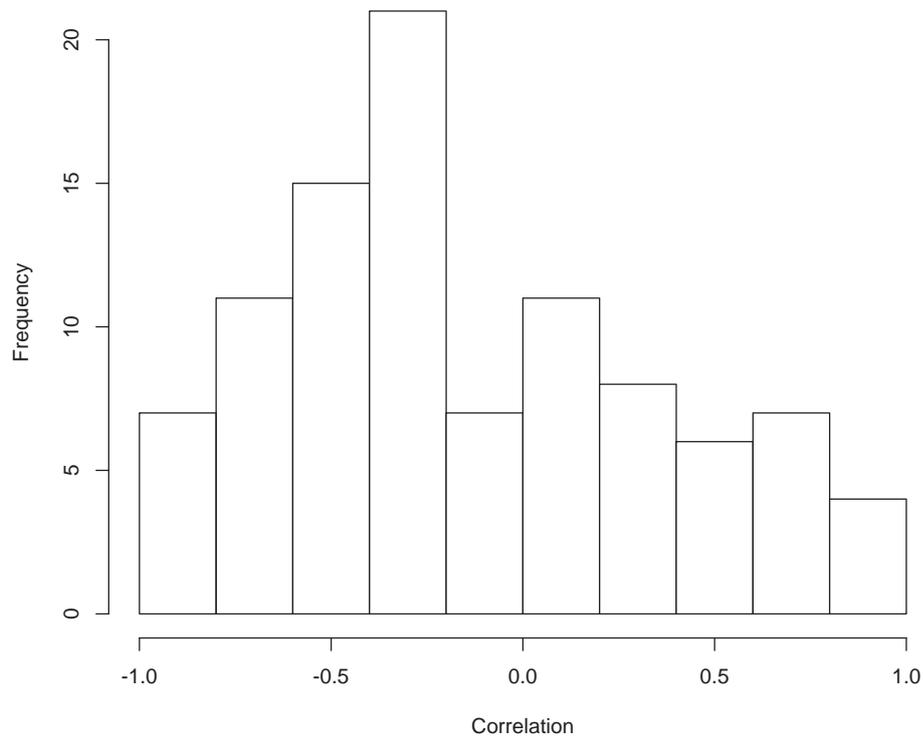


Figure 10. Frequency of correlations between log-transformed Psoriasis Area and Severity Index (PASI) score and serum calcidiol concentration across all participants with > 2 measurements of each ($n = 97$).

< 0 is an inverse correlation, 0 is no correlation and > 0 is a positive correlation.

Credit for graph: Dr M. B. Jones, Massey University.

6.1.1.Safety

There was no evidence of vitamin D toxicity in participants. All but one participant had serum calcium levels < 2.6 mmol/L at baseline, 3 and 12 months. That participant had an adjusted calcium level of 2.65 mmol/L (unadjusted level 2.35 mmol/L) at baseline, but levels at 3 and 12 months were < 2.6 mmol/L. One participant had slightly low serum calcium at 3 months (2.0 mmol/L). His doctor was advised (with the participant's permission), and levels were within the normal range at 12 months. No adverse effects of taking the capsules were reported.

6.2. Discussion

Topical analogues of vitamin D have been used to treat psoriasis for many years, but to the best of my knowledge, this is the first randomised trial aimed at determining whether oral vitamin D₃ significantly improves psoriasis compared to a placebo. The findings of this research are unable to support the use of oral vitamin D₃ as a treatment for psoriasis, as there were no differences in PASI scores between those taking 100,000 IU of vitamin D₃ a month and those taking an identical placebo when assessed at 3-monthly intervals over a 12-month period. However, these results are inconclusive when also considering serum calcidiol concentrations, as these increased not only in the treatment group from 3 months, but also in the placebo group from 6 months. On the other hand, analysis of the relationship between PASI scores and serum calcidiol concentrations across the whole sample suggests a benefit of higher serum vitamin D concentrations for psoriasis at a population level.

6.2.1. Increased serum calcidiol and a reduction in PASI in both groups

Both the treatment and placebo groups demonstrated similarly improved PASI scores compared to baseline alongside elevated serum calcidiol concentrations from between 6 and 9 months, albeit to a mild degree. It is difficult to interpret the meaning of these similarly reduced scores because of the increase in serum calcidiol in both groups, which meant that the difference in calcidiol between groups at 6 months was only ~25 nmol/L, and a discrepancy of this size is possibly too small to have allowed for detection of any beneficial effect of vitamin D. For instance, this difference was much smaller than the increase of 228 nmol/L in Finamor et al. (2013), in which marked improvement in psoriasis was seen, and even the ~65 nmol/L increase in UVB phototherapy trials upon which power calculations for this study were based (Osmancevic et al., 2009a; Vahavihu et al., 2010), and which showed a significant difference in psoriasis between groups. The increase in serum calcidiol in the placebo group was one of the clear limitations of this research, and is discussed further below. Yet, because both groups showed an overall improvement in psoriasis as well as an increase in serum calcidiol, it was

particularly important to determine whether any significant relationship existed between these factors across the whole sample of participants.

6.2.2. The significant inverse relationship between serum calcidiol and PASI

As the cross-sectional analysis showed an inverse relationship between PASI score and calcidiol concentration across the whole sample, this supports a benefit of higher serum calcidiol for psoriasis, at least at a population level. Although this is a secondary finding, it is also of importance, because while there is a strongly established link between topically applied calcitriol and psoriasis severity, propositions about a connection between serum calcidiol and psoriasis have thus far been tenuous. The findings of the present study are supported by those of Chandrashekar et al. (2015), Ricceri et al. (2013) and Bergler-Czop et al. (2016), who also found inverse associations between calcidiol and PASI ($n = 43$, $r = -0.71$, $p < 0.0001$; $n = 68$, $r = -0.88$; $p < 0.001$; and $n = 40$, $r = -0.43$ [significance not given], respectively). Similarly, Kincaid et al. (2015) found that those with moderate-to-severe psoriasis had significantly lower calcidiol concentrations than those with mild psoriasis (Q1: 32 vs. 45 nmol/L; median: 51 vs. 61 nmol/L; Q3: 75 vs. 84; $p < 0.05$ for all). Further, in a population-based study, those with more extensive psoriasis trended towards lower serum calcidiol in a multivariate analysis (-12.4 nmol/L, $p = 0.07$) (Wilson, 2013). Finamor et al. (2013) also found higher calcidiol achieved through oral vitamin D₃ supplementation predicted lower PASI scores ($r^2 = 0.32$, $p = 0.0153$) in their pilot study ($n = 16$). In studies in which no association between serum calcidiol and PASI score has been found (Gisoni et al., 2012; Orgaz-Molina et al., 2012), analysis was limited to one measurement of serum calcidiol and PASI from each person, and did not take potential confounders or individual differences into account. In contrast, the relationship observed in this study has strength because it was based on five regular observations over a 12-month period, and the analysis accounted not only for the repeated-measure nature of these observations, but also for the natural individual variation in psoriasis that occurs between people and the influence of several other confounders. This was important due to the variable nature of psoriasis, as well as the variability in the relationship between calcidiol and PASI that was

observed on an individual level. Our data also suggests the relationship between PASI and calcidiol may be non-linear, which could explain the lack of correlation found in some studies. Thus, the findings of the present study convincingly support the idea of a relationship between vitamin D levels and psoriasis severity.

6.2.3. The magnitude of estimated average improvement, and heterogeneity in the relationship between serum calcidiol and PASI

On the other hand, the estimated average improvements in PASI scores based on increasing serum calcidiol by up to 125 nmol/L in this study were very small from a clinical perspective, with the largest estimated average improvement following an increase of 125 nmol/L being 2.6 from an initial PASI score of 17.7. Yet, the model from which these estimated improvements were derived was based on a sample of individuals who had considerable heterogeneity among them in terms of the relationship between serum calcidiol and PASI. Firstly, correlation analysis at an individual level suggested that higher serum calcidiol was associated with lower PASI score only in two-thirds of participants, suggesting some might respond to elevated calcidiol concentrations, while others might not. Furthermore, of those participants who did show an inverse relationship, the degree of actual improvement in PASI between individuals was considerable, with 3.8% – 87.0% being the average range of observed improvement in PASI across all visits. While there was no difference in slope (i.e., effect of calcidiol on PASI) between individuals in our study, this may have been due to the small sample size. Of the participants who had improved by 3 months, only half ($n = 18$) still had some degree of improvement from baseline at all subsequent visits, perhaps reflecting aggravation of psoriasis by other unknown factors that overrode any benefit of vitamin D. Based on this apparent variability in the relationship between serum calcidiol and PASI, the estimated improvements should be considered as the average reduction in PASI that may be associated with elevating serum calcidiol across a population, with any individual improvements varying considerably around that average. It is therefore also possible that clinically significant improvements may be seen following elevation of serum calcidiol concentration in some individuals, while not in

others.

Heterogeneity in the relationship between psoriasis severity and vitamin D has previously been observed in the form of the widely variable response to both topical vitamin D analogues and oral calcitriol between individuals (Durakovic, Ray, & Holick, 2004; el-Azhary et al., 1993; Morimoto et al., 1986; Perez et al., 1996; Smith et al., 1988; Takamoto et al., 1986). A differentiation between “responders” and “non-responders” has been noted in relation to the clinical improvement of psoriasis following treatment with topical vitamin D analogues (Chen et al., 1996). In skin biopsies of treated skin, a large increase in keratinocyte VDR mRNA was seen in those who had clinical improvement of psoriasis, whereas there was no increase in VDR mRNA in those whose psoriasis did not improve (Chen et al., 1996), thus demonstrating a resistance to vitamin D as a treatment. Some studies have shown associations between VDR polymorphisms such as FokI, TaqI and Cdx2 and degree of response to topical vitamin D (Dayangac-Erden et al., 2007; Saeki et al., 2002; Zhao et al., 2015), but so far, findings between studies have been inconsistent (Sutherland, Power, Rahman, & O’Rielly, 2016). It is not possible to know whether participants in the current study differed either in VDR genotype or VDR mRNA expression, and it is not yet known why the relationship between serum calcidiol and psoriasis severity is so variable between individuals. Yet, people differ considerably in their response to any kind of psoriasis treatment (Almutawa et al., 2013; Nast et al., 2015; Samarasekera et al., 2013; Zweegers et al., 2016), and it is possible that variability in response to vitamin D between people with psoriasis is the outcome of a complex mix of genes involved in both the pathophysiology of psoriasis and the vitamin D pathway, both currently areas of research in which knowledge is limited. Until more is known in this regard, it might be useful to determine whether the relationship between serum calcidiol and PASI differs between those with different phenotypes of psoriasis, such the six classifications that have been suggested by Guinot et al. (2009), as these different phenotypes suggest differences in underlying genetic variability.

6.2.4. Consideration of the serum calcidiol concentrations achieved by participants

It is also possible that the serum calcidiol concentrations that were achieved by participants in this study might not have been high enough to lead to clinically significant improvements. Following on from the relative resistance to topical vitamin D analogues that some researchers have observed in relation to different VDR polymorphisms (Dayangac-Erden et al., 2007; Saeki et al., 2002; Zhao et al., 2015), it has been proposed that people with psoriasis might require higher serum calcidiol concentrations than the general population to compensate for this resistance (Finamor et al., 2013). To test this hypothesis, these authors gave 16 participants with psoriasis 35,000 IU of vitamin D₃ per day, increasing mean calcidiol from 46 ± 22 nmol/L to 331 ± 92 nmol/L and significantly improving PASI in each participant ($p < 0.01$), although again, the magnitude of improvement appeared to vary between participants (Finamor et al., 2013). Thus, it is tentatively possible that more significant improvements in psoriasis might be seen with higher serum calcidiol concentrations. Also, in regards to the 37% of people in the current study who did not demonstrate a relationship between serum calcidiol and PASI, it is not clear whether they are unresponsive to vitamin D, whether other unknown factors are overriding any potential effect of vitamin D, or whether they require a higher serum calcidiol concentration to see any effect.

6.2.5. The presence of a relationship between serum calcidiol and PASI across the range of serum calcidiol concentrations

Although the findings of the present study cannot demonstrate response or non-response to vitamin D at a cellular level, they do support the conclusion that the increased levels of systemic vitamin D were responsible for the improvements seen in psoriasis in both groups. This is because, in the subgroup that showed an inverse relationship between serum calcidiol and PASI, there was an equal proportion of people on the treatment and on the placebo, meaning that the relationship was present across both higher and lower concentrations of calcidiol. Had the relationship only been observed at higher calcidiol concentrations, it might have suggested that serum calcidiol was instead acting as a proxy for other benefits of sunlight. The presence of this

inverse relationship across the range of serum calcidiol concentrations also makes it unlikely that elevating serum calcidiol was only of benefit to psoriasis in those who were initially deficient in vitamin D (< 50 nmol/L), and instead suggests that increasing serum calcidiol may potentially be beneficial for psoriasis even when levels are already considered sufficient.

6.2.6. The question of how calcidiol in serum might benefit psoriasis

To clarify whether there is indeed a benefit of higher calcidiol concentrations for psoriasis, it would be helpful to elucidate the pathway by which increasing serum calcidiol might improve psoriasis. Keratinocytes possess the complete vitamin D pathway, allowing them to synthesise calcidiol and then calcitriol following exposure of skin to sunlight; calcitriol is then taken up via the VDR and utilised by the cell. Topically applied calcitriol is similarly taken up via the VDR. In contrast, it is not known whether keratinocytes are able to utilise calcidiol in serum as substrate for calcitriol. Lehmann (2009) has suggested that the amount of free calcidiol that is able to be taken up by keratinocytes is probably too low to allow formation of sufficient amounts of calcitriol, and that the majority of calcidiol is bound to DBP, and therefore too large to be incorporated into the cell. If this is the case, yet increased levels of serum calcidiol are found to benefit psoriasis, perhaps this benefit relates to the anti-inflammatory effects of vitamin D; that is, the hydroxylation of calcidiol to calcitriol, and the subsequent actions of calcitriol on immune cells (Baeke et al., 2010). Vitamin D is known to have powerful modulatory effects on the immune cells and pathways involved in psoriasis, including inhibiting the proliferation and activation of T-lymphocytes and altering the balance of Th1 and Th2 cells, thereby promoting a less inflammatory environment (Soleymani et al., 2015).

6.2.7. Serum calcidiol concentrations in people with psoriasis compared to the wider population

Some previous research has found people with psoriasis to have significantly lower serum calcidiol concentrations than healthy controls, although these findings have been limited to those with moderate-to-severe psoriasis (Bergler-Czop & Brzezińska-Wcisło, 2016;

Chandrashekar et al., 2015; Gisondi et al., 2012; Orgaz-Molina et al., 2012). In comparison, other studies have shown similar serum calcidiol concentrations between those with mild psoriasis and those without psoriasis (Wilson, 2013; Zuchi et al., 2015). Between 69% and 77% of our sample had mild psoriasis at any one time point, and mean serum calcidiol across the whole sample at baseline was comparable to the average levels in the New Zealand population (60 nmol/L vs. 63 nmol/L, $p = 0.19$), yet was lower than those living at a similar latitude in New Zealand (65 nmol/L, $p = 0.03$) (Mason et al., 2012). While comparison of serum calcidiol concentrations between different studies has been thought to be problematic due to the variability between different methods of analysis, the immunoassay used in the current study is positively biased (by 11% at 50 nmol/L) in relation to the HPLC method used in the population-wide study (Lippi et al., 2015), suggesting that the difference in serum calcidiol concentration between that found in our sample at baseline and the wider population may in fact be greater than 5 nmol/L. Regardless, these findings suggest that on average, people with psoriasis who have similar characteristics to participants in this sample may have insufficient serum calcidiol concentrations (i.e., < 75 nmol/L).

6.2.8. Strengths and limitations of this research

Strengths of this study were the high rate of participant retention, the size of the vitamin D₃ dose and the high reported compliance, which ensured there was a significant mean elevation in serum calcidiol and saw the majority of the treatment group achieving vitamin D sufficiency (see **Table 13**). However, there was still notable heterogeneity in the pattern and magnitude of change in calcidiol in response to supplementation on an individual level, something that has been observed in previous research (Castro et al., 2014). Well-established modulators of response to vitamin D supplementation are body fat percentage, baseline calcidiol (Mazahery et al., 2014) and age (Zittermann et al., 2014), and polymorphisms of the genes for VDR (Waterhouse et al., 2014), DBP (Fu et al., 2009) and enzymes involved in vitamin D metabolism (Didriksen et al., 2013) are also thought to have some effect. Establishing the predictors of change in response to vitamin D supplementation was not an objective of this

study, but was the focus of a follow-up analysis, alongside further consideration of the variation in change in serum calcidiol concentration between participants. These findings were written as a journal article (unpublished), which has been included as Appendix 29. This analysis showed that in those in the treatment group, the factors predicting a greater change in serum calcidiol between baseline and 12 months were lower body fat percentage and baseline calcidiol, older age and being of female gender. However, together these factors only explained 37.7% of the variance in change. As genetic factors were not measured in this study, their contribution to the differences in response is not known, nor is it known what other factors might have been involved; this is clearly an area for further research.

This study had a number of other limitations that made it difficult to interpret the findings. The most significant was the elevated serum calcidiol in the placebo group at 6 months, which made it impossible to determine whether vitamin D₃ supplementation had contributed to the small but significant improvement in PASI score in the treatment group. As the cross-sectional analysis suggested an overall benefit of higher calcidiol for PASI, elevated calcidiol in the placebo group at 6 months may have obscured a treatment effect, a notion that is supported by improvement in PASI alongside an attainment of vitamin D sufficiency in both groups at 9 and 12 months. The cause of increased calcidiol in the placebo group is unknown. That several participants reported increased sun exposure over the preceding three months suggests this could have been a contributing factor, although others for whom serum calcidiol increased reported no increased exposure, or even less exposure than normal. However, this assessment was very subjective and may therefore not be representative of true sun exposure, suggesting a more formal measure of sun exposure should have been used. Furthermore, some participants may have increased sun exposure subconsciously, particularly after having learned of the links between vitamin D and psoriasis. Wintertime in Auckland, New Zealand, provides decent sunlight hours with less burn-time than summer, making prolonged sun exposure possible. Also, participants were asked not to take any vitamin D₃ supplements during the study (other than those who had already been taking a multivitamin containing < 1000 IU per day upon enrolment, which would therefore not

lead to a sudden increase in serum calcidiol), yet it is possible some participants assumed they were on the placebo after the initial few months and decided to take vitamin D₃ regardless. Furthermore, the possibility that vitamin D₃ was inadvertently distributed to some placebo participants prior to their winter appointment also cannot be excluded.

The assessment of PASI and serum calcidiol five times per person over 12 months was a strength of this study, as it was intended that this would account for seasonal effects and somewhat compensate for the unpredictability of psoriasis. Yet, challenges with recruitment meant that people were enrolled during different seasons, and enrolment was not spread evenly across the year, which made it more difficult to interpret the changes in serum calcidiol in relation to supplementation and PASI scores. It was expected that a clear pattern of response would follow supplementation regardless of the baseline season (i.e., a sharp increase following baseline dosing followed by a plateau, with the size of the initial increase varying with season of enrolment), yet the pattern was more variable between people than expected. To avoid this, it would have been ideal to have limited enrolment to one season, probably winter, when calcidiol levels would naturally have been at their lowest. Recruitment and enrolment did begin in April of 2012 with an idealistic expectation of taking three to six months and thus covering the autumn/winter period; instead, it took 11 months, and thus the opportunity for common baseline seasons was missed. Despite this shortcoming, having five evenly spaced assessments of PASI and serum calcidiol over a 12-month period made the finding of an inverse relationship between these variables more robust, as did controlling for multiple confounding factors.

The sample size for this study was calculated based on improving PASI by at least 50%, at which quality of life tends to improve (Carlin et al., 2004). In hindsight, the degree to which this form of oral vitamin D (i.e., cholecalciferol), and potentially also the dose (as discussed above) might have an independent effect on psoriasis was possibly overestimated, particularly in light of the fact that use of other treatments (if already established) was permitted. If this were the case, a larger sample size would have been required to allow detection of any differences in PASI scores between groups.

One final limitation is that the finding of an inverse relationship between serum calcidiol concentration and PASI scores cannot be used to predict the benefit of increasing calcidiol for individuals, due to wide inter-individual variability in PASI scores. Also, it could not be clearly distinguished from this data whether any effect of vitamin D on psoriasis differed between individuals. However, these findings can be generalised at a population level comprising people with similar characteristics to those in this study.

6.3. Conclusion

As there were no overall differences in PASI over 12 months between those who were taking supplements of vitamin D₃ and those on a placebo, the findings of this study cannot support the hypothesis that taking vitamin D₃ supplements improves psoriasis. However, these results are also inconclusive due to the significant, unexplained average increase in serum calcidiol concentrations in the placebo group from 6 months onwards. These findings were also potentially confounded by the wide variation in individual response to supplemental vitamin D₃, with regards to change in serum calcidiol concentrations. Because of these complicating factors, a cross-sectional analysis of PASI scores and serum calcidiol concentrations was conducted and showed a mild but significant inverse relationship, suggesting that at a population level (versus an individual level), increasing serum calcidiol is associated with mild improvements in psoriasis. Previous research has shown significant improvement in individual PASI scores following very high doses (35,000 IU per day for 6 months) (Finamor et al., 2013), and it is possible that a higher dose of vitamin D₃ than used for the present study (200,000 IU, followed by 100,000 IU per month for a total of 12 months) might lead to greater improvements. Large randomised controlled trials using higher doses of vitamin D₃ would be needed to determine if higher calcidiol than achieved in this study produces greater improvements. Further investigation into factors affecting the response of psoriasis to vitamin D between individuals is also needed. As vitamin D appears to have an inverse relationship with psoriasis in a significant proportion of the population, maintaining desirable serum calcidiol

concentrations, currently undefined but at least a level of sufficiency (75 nmol/L) should be a factor in the management of psoriasis.

7. Conclusion

This thesis has been centred on two issues that are of ongoing importance in relation to psoriasis: the need for greater understanding of the experience of living with psoriasis from the perspective of the sufferer, and the need for safe, convenient and effective treatments. From these issues arose two aims, the first being to gain a deep understanding of how people make sense of living with psoriasis, and the second, to determine whether oral supplements of vitamin D₃ can effectively improve psoriasis. These aims are linked through the influence that the physical symptoms and appearance of psoriasis, as well as the characteristics of the treatments, have on the way a person experiences life with the disease. Due to the different epistemological assumptions and methodologies used to address these two aims, and because of how the overall project evolved in a chronological sense, this thesis has been presented in two separate parts. Study One was a qualitative study based on data from 10 semi-structured interviews, and involved an analysis of the narratives that participants used to describe their experience of living with psoriasis. Study Two was a randomised, placebo-controlled intervention trial assessing the impact of oral vitamin D on psoriasis severity in 101 people over a 12-month period. The purpose of this final chapter is to provide an overview of the main findings and contributions of this thesis, how these are situated within the context of the wider literature, the implications of these findings and the possibilities for future research that arise from them.

The major findings of Study One were the identification of three different dominant narrative forms that underpinned people's experiences of psoriasis, narratives of *restitution*, *resignation* and *chaos*, and an understanding of how these can interchange over time in relation to how a person perceives the severity and/or stability of their psoriasis. All participants used a restitution narrative to describe their experience of the years (or decades) following the onset of psoriasis, seeing it as something temporary and fixable, and focusing on finding a way to overcome it so they could return to 'normal'. When participants lost hope in overcoming psoriasis, yet felt the severity of their psoriasis was within the bounds of what they could cope with, they shifted to a resignation narrative. This involved attempts to push psoriasis to one side

and get on with life, begrudgingly accepting having to live with psoriasis and its ongoing challenges. In contrast, when a person's loss of hope in being able to overcome psoriasis was coupled with a perception that their psoriasis was too severe to cope with, they moved into a chaos narrative, where feelings of hopelessness, powerlessness and loss of identity prevailed. A shift away from a chaos narrative occurred when people took steps to gain an increased sense of control over their life, or, with a renewed hope in treatments, over their skin. These narratives and overall narrative trajectories highlight the key role that a person's ability to manage their psoriasis can play in shaping their experience of living with the condition, and thus these findings emphasised the importance of the research into vitamin D₃ supplementation as a treatment in the second half of the thesis.

The primary findings of Study Two were inconclusive: in the treatment group, monthly supplementation with 100,000 IU of vitamin D₃ over one year (200,000 IU at baseline) led to a significant increase in mean systemic vitamin D (serum calcidiol) concentration and a small but significant improvement in psoriasis (measured by PASI score). However, an unexplained increase in mean serum calcidiol concentration also occurred in the placebo group between 3 and 6 months alongside improvement in psoriasis, meaning it is not possible to draw any firm conclusions from these findings. On the other hand, a cross-sectional analysis of the relationship between serum calcidiol and PASI score across the whole group showed a significant inverse relationship existed between the two, meaning that in general, higher vitamin D levels are associated with less severe psoriasis.

At the time of publishing, this is the first known study to consider the narratives of people with psoriasis, and as such, it offers a new perspective from which to consider the experience of living with psoriasis. As was thoroughly discussed in Chapter 3, an extensive body of work has previously identified various specific problems and issues faced by people living with psoriasis, which include physical symptoms such as itching and flaking (de Korte et al., 2004; Globe et al., 2009), and psychosocial implications such as self-consciousness (Weiss et al., 2002), embarrassment (Sampogna et al., 2012) and feelings of stigmatisation (Hrehorow et al., 2012).

For the most part, these issues were also present within the narratives described in this research. However, very few studies have sought to understand the meanings such problems and issues hold for people's lives, or have gone beyond specific aspects of experience to consider life overall in any depth. The restitution, resignation and chaos narratives found in this study illuminate the ways in which people situate and give meaning to psoriasis and its challenges within their lives overall, and the various narrative trajectories show how these can shift and evolve over time. The current findings therefore make a significant contribution to the dermatological literature regarding psoriasis, where the study of narratives is essentially a new approach.

Furthermore, the findings of this thesis can be more broadly situated within the interdisciplinary body of work considering experiences of chronic illness, in which the study of narratives has been gaining traction in recent years. With regards to the experience of chronic illness in general, the identification of Frank's three narrative forms in experiences of psoriasis adds to their credence as possible canonical illness narratives and useful "listening devices" (Frank, 2013, p. 76). Also interesting in this regard was the persistence of the restitution narrative over a prolonged period of time, which challenges the assumption that a focus on a return to a prior state of good health is primarily the domain of those suffering from acute illnesses (Frank, 2013). In addition, this research identified and defined another form of narrative used by people with psoriasis, *resignation*, which is not well established in the literature and offers an understanding of another way that people can experience living with chronic illness.

The prolonged lengths of time over which people's experiences of psoriasis were told as unresolved restitution narratives also highlight the difficulty people have finding a treatment they deem acceptable. This finding aligns with previous research that has shown the considerable challenges that can be associated with finding an acceptable psoriasis treatment, not only with regards to efficacy, but also to side-effects, convenience and level of risk (Bewley & Page, 2011), with the challenges of treatment often significantly contributing to reduced quality of life (Pariser et al., 2016; Nash et al., 2015) and leading to feelings of lack of control

and powerlessness (Magin et al., 2009a). From another perspective, understanding the prominence and prolonged nature of the restitution narrative in experiences of psoriasis shows one way in which people respond to these challenges, in that they cultivate a sense of hope in being able to overcome the condition, as well as some sense of control over their situation. This is important, as having a sense of control over an otherwise incomprehensible, unpredictable condition such as psoriasis can promote a greater sense of wellbeing and confidence in life in general (Lamb et al., 2004), and having hope provided motivation in regards to adherence to treatments. However, as hope could also be potentially devastating when pinned on an outcome that never arrives, such as clear skin in psoriasis, it seems pertinent that healthcare practitioners support their patients to foster hope grounded in realistic outcomes, alongside giving them the best opportunity to succeed in their attempts to manage their condition.

The findings of this research show that when psoriasis is perceived as being severe and uncontrollable, people can suffer an extreme loss of self-confidence and self-esteem leading to a withdrawal from participation in everyday life, and the sense that psoriasis has taken over their sense of identity. Probably because psoriasis is not usually life-threatening, its impact on people's lives can often be underestimated both by healthcare professionals (Bewley et al., 2014) and by people in general (Jobling & Naldi, 2006), yet the significance of these consequences for a person's life stresses the importance of being aware of the potentially serious impact of psoriasis. The experiences of participants who told chaos narratives suggested that one of at least two approaches helped them to regain a sense of power, hope and identity, and it may be that they could also help to prevent such suffering. One scenario involved renewal of hope that effective management of psoriasis was possible, and from a healthcare perspective, this would mean ensuring that people with difficult-to-manage psoriasis, especially if they are exhibiting signs of distress, have access to the full range of treatment options to give them the best chance of success in this regard. The second scenario involved gaining a greater feeling of empowerment in relation to psoriasis through the development and implementation of general self-care skills, such as focusing on looking after one's own physical and emotional

wellbeing. Interestingly, for the two participants who followed this path, better self-care coincided with an improvement in their psoriasis, which then helped them to accept it. The findings of this study therefore suggest that by strengthening their sense of control in relation to their own health, people are better able to accept their psoriasis and have less fear about potential exacerbations in the future. On the other hand, with a renewed search for treatments, the avoidance of suffering depends of the success of the treatment, and the person also lives in fear of it returning because a sense of control around their health has not been developed. What might be ideal is a combination of these two strategies, where the person is supported to develop self-care strategies alongside their treatment efforts.

Regardless of the degree of acceptance, the narratives presented in this study showed it was not easy for people to live with psoriasis. At best, it was begrudgingly accepted, and presented ongoing hassles around management and/or self-consciousness about appearance and fear of stigmatisation. These findings raise the question of how people with psoriasis might be supported to have a less negative experience of living with the disease, particularly while the effectiveness and convenience of treatments, especially for people with mild psoriasis, remains limited. The belief that the appearance of psoriasis was socially unacceptable and the fear of judgment from others, aspects of psoriasis that have been noted previously (Magin et al., 2009a; Magin et al., 2011), were central to the narratives presented in this study. Alongside the ongoing need for development of effective, safe, convenient and widely available treatments for psoriasis, it therefore seems crucial to foster a social environment in which people feel their psoriasis is accepted by others. This implies the need for an increase in public understanding and awareness about what psoriasis is (i.e., a non-contagious, immune-mediated condition) and how challenging it can be for people to live with it. While a change in public misconceptions around psoriasis will undoubtedly require a large-scale effort over time, the impact on individuals with psoriasis shows how important it is that the persistent social stigma towards psoriasis is ultimately eradicated.

Finally, the narratives presented in this study are based on people's experiences that are often withheld due to feelings of embarrassment and a perceived lack of understanding from others. Yet, understanding can only increase through the sharing of such experiences. Hopefully, people who feel isolated as result of having psoriasis will recognise some of their own stories in these narratives, and see their presentation as part of gradually overturning public misconceptions about the disease and increasing awareness of how it can impact people's lives. Relatedly, several studies have identified the struggle that people with psoriasis have to feel understood by physicians who focus on symptoms and management, and limit their opportunity to express how psoriasis affects their lives overall (Nelson et al., 2013; Errser et al., 2010). In particular, people have expressed a need for physicians to acknowledge their patients' feelings of lack of control in relation to psoriasis, and the stigma that is associated with living with a visible disease (Nelson et al., 2013). As alluded to earlier in this chapter, it has been proposed that understanding the narrative forms that people use when they talk about their illnesses encourages closer listening, and helps people to hear different narrative threads in the story that can otherwise be difficult to make sense of (Frank, 2013). For this reason, the findings of this research may allow others, and especially healthcare providers, to better comprehend these experiences and to therefore be able to provide more relevant support to people who are struggling with the disease.

The narratives and narrative trajectories identified in this study were based on the experience of ten particular people, and it is possible that by interviewing others, different types of experiences would be identified and further increase understanding of the experience of psoriasis. Furthermore, participants in this study had a relatively similar demographic background, and future research focusing on different sociodemographic and ethnic groups would likely identify different understandings specific to those groups. In general, further research focused on gaining a greater understanding of how people might develop a more positive acceptance of psoriasis would be beneficial for its practical applications.

This research also raised questions around the different experiences of people living with psoriatic arthritis. While psoriatic arthritis was not an initial focus of this study, two participants gave detailed descriptions of their time living with this condition because of its inherent relationship with psoriasis. Each woman used the same narrative trajectory (from chaos, to resignation, to the emergence of quest) in describing their experience of psoriatic arthritis, and this similarity might have been due to having been through comparable life experiences in general, and to their dispositions being rather alike. Thus, interviews conducted with a larger group of participants (both men and women) with psoriatic arthritis would elucidate a more thorough understanding of narrative forms used in the experience of this condition.

The known challenges around managing psoriasis with available treatments and the need for an effective, safe and convenient treatment option were the motivating factors behind Study Two, alongside the evidence suggesting that increasing systemic vitamin D levels using vitamin D₃ supplements might improve psoriasis severity. Findings of a recent, uncontrolled pilot study had suggested promise in this regard (Finamor et al., 2013), but to the best of my knowledge, this was the first randomised controlled trial conducted to assess the efficacy of vitamin D₃ supplements on psoriasis compared to a placebo. The inconclusive primary findings of this study highlight an immutable challenge of conducting research into vitamin D supplementation, which is that unlike for other nutrients, levels of vitamin D cannot be controlled by intake as they are primarily influenced by sun exposure (Holick et al., 2011). Thus, the unexplainable increase in serum calcidiol concentrations in the placebo group meant that the findings of this study cannot progress research forward to the point of identifying whether or not vitamin D supplementation can improve psoriasis, and this still remains an unknown. However, the main implication of this research is the support that the secondary analysis provides for ensuring adequate vitamin D levels are a focus of clinical enquiry in people with psoriasis, as well as for pursuing the investigation into the relationship between serum calcidiol and psoriasis severity. The current findings add further strength to the evidence from several previous studies in which

significant inverse correlations between psoriasis severity and serum calcidiol have been observed (Chandrashekar et al., 2015; Ricceri et al., 2013; Bergler-Czop et al., 2016; Finamor et al., 2013). The findings of the current study could be considered as stronger than those of previous studies, as this analysis was conducted in a larger sample ($n = 101$ vs. $n = 9$ to $n = 68$); the relationship was assessed across five different time points rather than just at one or two time points; and unlike in straightforward correlation analysis, a range of effect modifiers and confounding factors were accounted for, meaning that the findings describe the unique relationship between serum calcidiol concentration and PASI score. While at the levels of vitamin D achieved in this study, the estimated improvements in PASI score based on increasing serum calcidiol were only minimal and unlikely to be clinically significant, the findings of this research also suggest that a relationship between psoriasis and vitamin D may be present for some people while not for others, therefore further investigation is warranted due to the possibility that clinically significant effects could be seen in some (as yet undefined) subgroups. The wide variability in the change in PASI score amongst those for whom there was an inverse correlation between serum calcidiol and PASI, as well as the apparent lack of correlation in some people, also suggests a benefit of further investigation into how and why people with psoriasis may differ in response to vitamin D at a cellular level.

Furthermore, as there was no evidence of a threshold effect above which levels of systemic vitamin D appeared to improve psoriasis to a greater extent, and the estimated improvements appeared to be greater at higher levels, it would be useful for future research to assess the impact on psoriasis of attaining higher average serum calcidiol concentrations than were achieved in this study. Relatedly, although this research supports the dosing regime of 200,000 IU of vitamin D₃ at baseline followed by 100,000 IU a month in enabling the majority of people to safely achieve and sustain vitamin D sufficiency, further elucidation is needed around why people respond so variably in terms of serum calcidiol following vitamin D₃ supplementation.

This research also offers several methodological implications to consider for any future investigation into the effect of vitamin D supplements on psoriasis. Firstly, the sample size: this

study was powered to detect a 50% reduction in PASI, which was probably too optimistic alongside concomitant use of other treatments and perhaps also with the dose of vitamin D that was used. As a year-long trial might be ideal due to the fluctuations that occur in both vitamin D and psoriasis, particularly with the seasons, yet as it is likely to be difficult to recruit an adequate number of people for a trial of this length without permitting some treatment use, a similar study should be powered to detect much smaller improvements in PASI and thus would require a greater sample size. Secondly, the frequency of assessment: the fluctuations in vitamin D and psoriasis provide a good justification for frequent assessment of serum calcidiol and PASI, as was done in this research, rather than just at baseline and endpoint. In this study, having numerous regular measurements strengthened the finding of an overall association, and in a comparison between groups, it could indicate the approximate timing of any effect, and determine whether there is any difference in short-term compared to long-term change. Thirdly, timing of enrolment: participants should ideally be enrolled during the same season, or at least evenly across the year, to allow more straightforward interpretation of the changes in serum calcidiol following supplementation, and any corresponding changes in PASI. Finally, the challenge in interpreting the findings in this study due to the unexpected elevation of serum calcidiol in the placebo group provides further argument for same-season enrolment, and, as it would be impossible (and unethical) to require participants to limit their sun exposure over a year, it suggests the need for formal, objective assessment of sun exposure, as well as exclusion of those who intend to holiday to a sunny destination.

The organic nature of the chronology of the two studies presented in this thesis meant that they did not cross over in a practical sense, in that they were conducted with different groups of participants, and the method and findings of each study were not directly integrated with the other. Yet, their connection lies within the ‘bigger picture’ of psoriasis, one in which human experience is at the centre, and where any investigation into treatments and whether they are successful at improving psoriasis or not has a potentially influential role on the nature of this experience. Previous research into psoriasis has thus far been primarily conducted within two

rather separate areas, one that focuses on deepening understanding of the experience or burden of living with psoriasis, and the other that focuses on psoriasis and its treatments from a biomedical perspective. Recent discussions in dermatology have begun to stress the importance of integration of these areas (Nelson et al., 2015; Jobling & Naldi, 2006), which acknowledges firstly the importance of treating a *person* who has psoriasis, as opposed to trying to treat psoriasis in isolation from that person; and secondly, the importance of understanding a person's background and experiences when treating their psoriasis in order to provide them with the most appropriate care (Nelson et al., 2015). This gradual shift is in line with that which has been proposed in relation to illness in general, particularly those that are chronic (Kleinman, 1988; Charon, 2012). As a focus of future research, then, it is proposed that these two perspectives (experiential and biomedical) should be deemed more than just complementary; in fact, each can be seen as able to inform and enhance the other. For example, gaining deeper insight into the meaning of the ongoing difficulties faced by people with psoriasis (e.g., physical symptoms, specific challenges with treatments) could support the development of potentially more acceptable treatment options, and findings from biomedically-focused research (e.g., the variability in participant responses to treatments) could contribute to a greater appreciation of what people with a particular illness are living with. In other words, such a mixed method approach has the potential to enrich understanding of both psoriasis as a biomedical condition and the personal experience of living with psoriasis. Future investigations into psoriasis treatments could possibly even involve consideration of the impact of the nature of experience when determining so-called objective outcomes.

To finish, this thesis has considered two aspects of psoriasis that, at face value, may seem somewhat disparate. However, the investigation into vitamin D as a treatment for psoriasis, as was discussed in the second half of this thesis, became the inspiration for the research that was ultimately presented as the first half, in which a greater understanding of the experience of living with psoriasis was sought. Along with offering insights into how people make sense of their psoriasis, the first part of this thesis therefore also further emphasised why the second half

of this thesis mattered. As has been set out several times in this thesis, the impact that psoriasis can have on a personal level is becoming more widely appreciated, but there are still gains to be made in terms of this appreciation becoming more widespread. Similarly, the relationship between systemic vitamin D and psoriasis severity remains in the preliminary stages of being understood. Approaching future research by combining efforts to uncover new biomedical understandings with a focus on the experience of the sufferer would be an important step towards being able to meet the needs of people with psoriasis. It is hoped, therefore, that the findings of this thesis are able to contribute to the progression of these areas of need.

8. References

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Appendices: Study One

Hello,

My name is Michelle Ingram, and I am a PhD candidate within the School of Psychology. I am undertaking research on chronic plaque psoriasis, a non-contagious inflammatory skin condition.

The aim of my research is to explore people's experiences living with psoriasis. I am interested in hearing how having psoriasis has affected their lives, in any sense.

I am looking to interview around 10 people who are happy to share their experiences of living with psoriasis, and who meet the following criteria:

- have had chronic plaque psoriasis for more than 2 years
- have had their psoriasis diagnosed by a dermatologist
- are aged 18 years or older
- who are based in the Wellington region

The interviews will take place in a private room on the Massey University campus in Wellington, and will take around 1 – 1 1/2 hours. The interviews will be digitally recorded and then transcribed, and participants can ask questions and clarify any issues they may have about the project at any time.

This study will be one of only a few that have taken a qualitative approach, which allows people's stories and experiences about living with psoriasis over an extended period of time to be captured in a more personable, in-depth way. I am hoping this research will contribute to a respectful awareness about the challenges associated with psoriasis, and help in demystifying the condition to those who don't suffer from it.

If you are interested in being involved, I would very much like to hear from you! Please provide your contact details via email and I will be in touch: m.ingram@massey.ac.nz

This research project has been approved by the Massey University Human Ethics Committee: Northern - MUHECN 12/076.

Best wishes,
Michelle Ingram
PhD Candidate
School of Psychology
Massey University
m.ingram@massey.ac.nz



The *Psoriasis* Study



Living with Psoriasis

Information Sheet

My name is Michelle Ingram, and I am currently undertaking a PhD at Massey University. As part of my PhD, I am conducting research into what it is like to live with psoriasis, under the supervision of Professor Kerry Chamberlain from Massey's School of Psychology.

What is this project about?

The aim of this study is to explore people's experiences of living with psoriasis. I am interested in hearing about how psoriasis has affected your life, and I would like to invite you to participate in this interview-based research. It will involve meeting with me for a one-on-one interview about your experiences. The interview will take place in a private room at Massey University in Wellington. I intend to conduct individual interviews with about 10 people.

The interview is likely to take about 1 – 1 ½ hours, and will be digitally recorded and then transcribed. You can ask questions and clarify any issues you may have about the project at any time, and can withdraw your participation up to one week after the completion of the interview. During the interview, you don't need to answer anything you don't want to, and we can turn the voice recorder off at any time.

While I would value your contribution to this research, you are under absolutely no obligation to take part. I recognise that talking about your experiences may not be easy, and if you do decide to be part of this project, I will do everything I can to make sure this is a safe, respectful and hopefully interesting experience for you.

How will your information be used?

All information you provide will be treated as confidential. You will not be identified by name on any of the transcripts, and this information will be used solely for this study. Your contact details and consent forms will be stored separately at Massey University to protect your confidentiality and I will be the only person who knows who you are. The interview recordings will be destroyed as soon as the analysis is completed. The transcripts will be stored securely for five years with all identifying information removed, and will then be destroyed, as required by research protocols.

You can choose to have a summary of the findings sent to you at the end of the project. Please indicate on the Consent Form if you would like to receive this summary.

Please feel free to contact myself or my supervisor if you have any questions about this project.

Michelle Ingram

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Committee Approval Statement

This project has been reviewed and approved by the Massey University Human Ethics Committee: Northern, Application 12/076. If you have any concerns about the conduct of this research, please contact Dr Ralph Bathurst, Chairperson, Massey University Human Ethics Committee: Northern, phone 09 414 0800 ext. 9570, email humanethicsnorth@massey.ac.nz



MASSEY UNIVERSITY
ALBANY

27 September 2012

Michelle Ingram
c/- Professor K Chamberlain
College of Humanities and Social Sciences
Massey University
Albany

Dear Michelle

HUMAN ETHICS APPROVAL APPLICATION – MUHECN 12/076
Life with Psoriasis: A Qualitative Study

Thank you for your application. It has been fully considered, and approved by the Massey University Human Ethics Committee: Northern.

Approval is for three years. If this project has not been completed within three years from the date of this letter, a reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely

Dr Ralph Bathurst
Chair
Human Ethics Committee: Northern

cc: Professor K Chamberlain
College of Humanities and Social Sciences
Dr P von Hurst
College of Sciences



School of Food and Nutrition
Massey University
Eastbourne Road Building 22
Gate 4, Oteha Rohe Campus
Albany 0632
Auckland



Living with Psoriasis

PARTICIPANT CONSENT FORM

This consent form will be held for a period of five (5) years.

I have read the Information Sheet and have had the details of the study explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time.

I would like to participate in the proposed study and be interviewed about my experience with psoriasis. I understand that I can decline to answer any questions and can stop the interview at any time.

I agree to participate in this study under the conditions set out in the Information Sheet.

Signature: **Date:**

Full Name - printed

I would like to be provided with a summary of the research findings: YES / NO

If you have requested a summary of the research findings, please provide your email address below:

Email: _____

Focus: How has having psoriasis impacted your life? [from the past to the present]

[Check participant is comfortable, do they want a cup of tea?]

Thank you so much for offering to speak with me today and giving up your time to do so. I am conducting these interviews to try and learn about the ways that having psoriasis can affect a person's life.

I just want to remind you that everything you say in this room will be kept confidential, unless you explicitly request otherwise, or if there is concern for your safety.

After we finish the interview, it will be transcribed by me, and I will use a pseudonym to protect your identity. If you decide to change your mind about taking part, you will be able to withdraw from the study within a week of this interview taking place [state day].

Please remember that you don't need to answer anything you don't want to, and we can turn the voice recorder off at any time.

[Give consent form for signing]

I am interested in hearing your stories and experiences about living with psoriasis. As we get into the interview, I may ask a few questions here and there but will mainly follow your lead with what you would like to share with me.

[Check ok to turn voice recorder on]

Preliminary Questions

Can you tell me a bit about yourself? [including...

Age?

Married?

Children?

Siblings?

Work?

Length of time with psoriasis?

Who made the diagnosis?

Prompts for Experiences with Psoriasis Interviews

Can you tell me about when you first realised that you had psoriasis?

- What was happening in your life at the time?
- How did you react to your diagnosis? What did you think/how did you feel?

When did having psoriasis become an issue for you?

- What happened?

- Have you done anything to try and manage it? [treatments etc]
 - Why/why not?
 - Was it helpful?
 - How have you felt about the treatments you have used?
 - How do you feel about treatments going into the future?
- Do you talk about your psoriasis with people - family / friends?
 - Why / why not?
- How did your family / friends react when you were diagnosed?
 - How did this make you feel?

What is it like for you now, to have psoriasis?

- If anything has changed, why?

How do you feel having psoriasis has affected your life?

Has having psoriasis affected your relationships with others?

- In what ways?
- Romantic/platonic?
- Has it affected the way you interact with people?

Has having psoriasis affected your work life?

- In what ways?

Are there any other ways in which psoriasis has been a challenge for you?

Have you found any positive aspects of having psoriasis?

Other possible reflections [if not covered already]

- How do you feel about your psoriasis?
- How do you see psoriasis in relation to yourself?
- Has the way you think about your psoriasis changed over the years? In what ways?
- Do you have any thoughts about why you got psoriasis?
- Do you think your life would have been different if you did not have psoriasis? In what way/s?
- How do you see your future with psoriasis?

Wrap up / voucher

Cara

Cara is in her mid-30s and works in administration. She has a supportive partner, and her life is centred on her two young girls. She is also close with her mother and grandmother, who live nearby. Cara has a bright, bubbly personality and laughs a lot, yet doesn't have much of a social life, which she puts down to the fact that her children keep her busy. She comes across as warm and friendly.

Cara's psoriasis history

Cara has had psoriasis for almost half her life, since she was about 18. It is mainly restricted to her scalp, with a little bit on her back, and so not visible to others, although the flakes are. Her scalp is often intensely itchy, has a burning sensation and flakes profusely. Following her diagnosis, her doctor gave her a short course of oral prednisone, but she didn't finish the course as it made her feel too ill. She has tried a range of topical treatments over the years, but has not found them to be effective apart from sometimes providing temporary relief. As they are a hassle to apply, she now only uses a treatment if she is desperate for relief, and she avoids buying new treatments because of wasting so much money in the past on ones that have been ineffective for her. Instead, she has tried to develop her own mental coping mechanisms for controlling the itch.

Cara's storyline

Following her diagnosis, Cara was hopeful she could permanently get rid of her psoriasis by diligently applying topical creams. Over time, however, she realised that these treatments could only provide temporary relief at best, and that she was unlikely to ever be rid of her psoriasis. She therefore decided the only way she would be able to cope with her condition was to develop her own coping mechanisms. With regards to managing the itch, she has been successful to some degree, for instance by training her mind to be able to ignore it. Yet the constant flakiness and potential visibility of her psoriasis has seemed to her impossible to get on top of; despite her all-consuming attempts to keep her appearance in check, the flakes so quickly and unpredictably return. As a consequence, Cara is plagued by persistent feelings of self-consciousness, always worried about what other people are thinking about her. While she tries to take responsibility for her self-consciousness, she also feels powerless to change it. She sees only two solutions that will allow her to live free of self-consciousness: one relies on someone developing a cure for her psoriasis, which is out of her hands and is seemingly impossible; and the other would require talking to others about her psoriasis so that they understand, which also seems impossible as she sees such talk as being socially unacceptable. Overcoming her feelings of self-consciousness while her psoriasis remains as it is is not seen as an option. Therefore, Cara does not see the future as holding much in the way of improvement for her situation, and her experience with psoriasis has led to feelings of guilt that she may have passed it on to her daughters, and that they may have to go through a similar thing. Despite this, she remains upbeat, tells herself that things could be worse, and tries not to let it bother her too much.

Logan

Logan is in his early 50s. He is creative, homosexual, and is single with no children. Logan has a wry sense of humour and appeared slightly nervous at the beginning of the interview, but once he began speaking, was eloquent and thoughtful, and I felt, open.

Logan's psoriasis history

Logan developed psoriasis around the age of 10. It began mostly on his scalp, and he treated it using coal tar and a lot of combing. It worsened following his adolescence, and it spread to other parts of his body, including his torso, hands, face and genital area. He experienced quite heavy plaque, especially on his knees, which would bleed when he bent his knees. He developed psoriatic arthritis over one summer in his 20s, which also affected his knees, but that was the only time it caused him any pain or problems. He has been on and off different systemic treatments over the years, and did PUVA treatment for a long time. Some of the systemic treatments caused side effects he wasn't happy with, and the PUVA became more of a hassle than felt necessary, as his psoriasis had reached a point when he thought he could manage it with creams. The severity of his psoriasis noticeably declined when he took up exercising and lost a lot of weight about ten years ago. For the last couple of years, he has been taking methotrexate, and has had reasonable success and only mild side effects with this. He also continues with his rigorous long-term regime of removing plaque from his face and facial hair every second day.

Logan's storyline

Although Logan had psoriasis from the age of 10, it began to have a significant impact on his self-esteem as its severity worsened during his late teenage and early adult years. Despite doing his best to treat and hide his skin, he has found no apparent solution to overcoming his self-consciousness in intimate situations, where his skin is, by nature, exposed. With a perceived lack of options to overcome this self-consciousness, Logan has held himself back from opening up to others and being vulnerable and available. This has resulted in an absence of meaningful romantic relationships and a painful gap in his life. Logan blames his psoriasis for having marked him, as his sense of self-consciousness has become embedded in his personality. Because of how majorly he felt psoriasis had shaped his life, and how negatively he felt about himself as a result, he realised he needed to start thinking about his psoriasis in a particular way and to confront it somehow. This was Logan's first step towards reclaiming some of the power that he felt psoriasis had had over him. He began trying to approach his psoriasis with curiosity and creativity, for example, by gathering in to a jar, or by laughing at the strange ways it manifests. The second step was when he decided to change his approach towards his overall health by starting to exercise. By taking action to improve his overall health, Logan moved from a place of feeling disconnected from and powerless in relation to his own body, to a place where he was able to start recognising his own power to take care of himself. He has maintained this lifestyle for the past decade, along with following a treatment regime for psoriasis that keeps his psoriasis to a minimum, and this has meant that he now feels generally positive about life and the future. However, he still grapples with residual elements of the long-lived, earlier effects of psoriasis, such as feelings of self-consciousness about visible plaques, automatic judgment and self-rejection of his own physical appearance, and the pain of the culmination of years of longing for a meaningful intimate relationship. He still has the jar containing flakes of skin, and this has taken on the function of helping him try and make sense of the way he is and the habits and personality traits that he has formed because of psoriasis. He is working towards acceptance of himself through being able to accept his condition as a part of himself and acknowledging its contribution to the person he has become.

Tessa

Tessa is in her late 50s, is married with adult children and owns her own business. Along with psoriasis, Tessa also has diabetes, thyroid issues and high blood pressure, and is overweight. She comes across as very open and chatty with a wry sense of humour.

Tessa's psoriasis history

Tessa has had psoriasis for around thirty years, since her late twenties. It started on her scalp, but it also affects many different areas on her body (arms, legs, torso, scalp) and causes her intense itchiness and profuse shedding of scales, especially on her scalp. She spent years unsuccessfully trying a range of different topical creams and lotions, which were either ineffective or caused a bad reaction and made the plaques worse. She was put on ciclosporin at one point, and while it completely cleared her skin in a very short time, she experienced a medical emergency due to an infection and the emergency doctors told her to stop taking it. Since then, she has avoided conventional treatments and has been using moisturiser for the dryness, while trying to figure out a cure; she thinks this might be found by looking at the food she eats.

Tessa's storyline

Tessa's psoriasis plays a major role in her daily life, causing her a great deal of frustration and embarrassment. As a consequence, she spends a lot of time and energy trying not just to treat it, but to overcome it. Following her diagnosis, the intense itchiness and flakiness of her scalp motivated her to try every topical treatment available, but nothing has worked. Her desperation for a treatment to work began to mount, and she even shaved her head in the hope it would help – but it didn't. As she told her doctors that she reacts badly to some of the treatments yet they continued to prescribe them anyway, she begins to mistrust her doctors. Since she hasn't responded to the treatments, she also begins to question whether they have diagnosed her correctly and if she has psoriasis at all. The appearance of psoriasis on the rest of her body is not an issue for her until she experiences negative reactions from several people on one day. Feeling angry at being so judged, she begins to hide her psoriasis when in public to avoid causing such a reaction. When her skin was cleared using ciclosporin, she felt liberated. Yet the severe side effects and the hospitalisation that soon followed was the last straw for her and conventional treatments. She has since refused to believe there is no cure for psoriasis, and suspects that there is probably a simple answer that has been held back from the public by big pharmaceutical companies. Her feelings of injustice on behalf of herself and the wider population have been amplified by watching a film about sugar in the food we eat; through seeing this film, she concludes that she has been duped about the quality of the food she eats, that all the efforts she has made to eat well have been in vain, and that too much sugar in the food supply is the likely cause of her health issues. As a result, she is now on a mission to remove sugar from her diet, which she nearly despairs at the challenge of, and to find a cure for her psoriasis. She dreams of widely sharing the cure with all those who need it, because she knows how much suffering they can go through, and to spite the big companies.

Jane

Jane is in her late 50s. She is in a long-term relationship and has a teenage son. She has a passion for the arts and is working towards becoming a therapist. She loves keeping active by going for long walks and being in the outdoors. Jane has had a challenging life, especially during her childhood and adolescence, and she has undergone therapy to work through her difficult experiences. Along with psoriasis and psoriatic arthritis, Jane has also struggled with depression and anxiety throughout her life, and she groups these together as being part of the same auto-immune condition. She also has osteoarthritis. Jane comes across as a gentle, kind woman, who is a little nervous and reserved at first, but warms up during the interview.

Jane's psoriasis history

Jane has had psoriasis on her skin since she was five years old, and was diagnosed with psoriatic arthritis three years before the interview. Her psoriasis was severe at first, affecting large areas of her body. She was treated as an outpatient for a number of years, but only remembers using topical treatments. Her skin improved over time, and it is now limited to smaller patches on areas such as her hands and legs. While it tends to always be present to some degree, she only uses treatments on her skin now if it is painful. Her recent diagnosis of psoriatic arthritis was made after she fell down stairs and broke her wrist, and was referred for tests as her fingers were not recovering as they should have been. Since the diagnosis, she has been taking arthritis medication, but she now finds it challenging to walk for more than short periods, and has also gained a lot of weight.

Jane's storyline

Jane does not consider the psoriasis on her skin to have been a major concern during her life, and she puts this down to having experienced trauma during her childhood, which made her feel numb, and that all other memories are muted in comparison. That said, she acknowledges that she has always put her physical self 'to one side', and partly relates this lack of body confidence to her psoriasis: because she views her skin as ugly, she views herself as ugly. She also sees her psoriasis as a reason why she has always dressed to hide herself, and this has become such a habit that she doesn't even think about it. Through therapy, Jane worked through her early experiences and developed more confidence in herself and her life direction. She spent many happy years working as a musician, building a family and living an active life. As a musician, particularly, she always felt as if there was a barrier between her technical ability and reaching her potential. Her response to her diagnosis of psoriatic arthritis was to feel angry and bitter, as she saw it as threatening the things she holds to be important, such as her youthfulness and her physical capabilities. Yet she also realised she must have had it for most of her life, and therefore her diagnosis also helped her to make sense of why she had never been able to break through that barrier with her music. Jane has used the strong inner resources she has developed through overcoming hardships in learning to live with her psoriatic arthritis diagnosis. She realises she has to adjust her approach and attitude to life in order to accept her arthritis and be happy. In accordance with this, she is actively trying to alter the story she had imagined for how the rest of her life would go, so that it accounts for the arthritis but still makes her feel happy. While she is still in the process of accepting the arthritis, and getting used to the treatment, she is determined for it not to be an issue for her, and has confidence she will be able to do so.

Carrie

Carrie is in her early 40s. She is a health professional and works in a hospital. She is homosexual and has a supportive long-term partner. Carrie is a very introspective person and a seeker of knowledge, and is always looking for ways to understand herself and the world around her more deeply. She comes across as warm, open and reflective.

Note: Carrie was part of the randomised controlled trial that took place in Auckland between 2012 and 2014, during which she had expressed enthusiasm in taking part in these interviews. It was clear that she had a story to tell, and messages she wanted communicated to a wider audience about her experiences with receiving treatment for psoriasis. It turned out that she had been on the placebo capsule for the year-long duration. This was especially significant in light of the interview that we had, as she described the time leading up to and during that trial period as essentially a period of reaching rock bottom for her with regards to her psoriasis, and by extension, her life. This was not apparent at the time, although I was aware she was unhappy with her skin's condition. The narrative she told offered a great deal of insight into the implications of taking systemic and biologic treatments for her, and of the reasons why she chose to do so.

Carrie's psoriasis history

Carrie's psoriasis first appeared when she was around the age of 28. It spread gradually at first, and then stayed stable for years, mainly affecting her torso. During this time, she tried different approaches such as using non-steroidal creams, eating well and just trying to ignore it, but her skin did not improve. About eight or nine years later, the severity of her psoriasis increased dramatically, quickly becoming more widespread. She aggressively applied topical steroids in the places the psoriasis was visible – her lower arms and face – which helped her to knock it back a bit, but also caused damage to her skin. She began to feel unwell, like she was constantly dehydrated, her skin felt like it was burning and she starting to have pain in her joints and muscles. She began to take systemic medicines, which led to varying degrees of improvement for her skin and resolution of her other physical symptoms. However, she experienced significant side effects, including nausea, dizziness, extreme fatigue, peeling of skin from her hands, and worryingly high blood pressure, and so she could not stay on systemics long-term. Therefore, she was prescribed biologics, the second of which she responded to well enough to be able to continue her prescription. While she still gets new lesions appearing in places, the biologics have now helped her maintain minimal psoriasis for just under a year.

Carrie's storyline

Carrie sees psoriasis as an external symptom of an inner emotional issue, and therefore takes some responsibility for its presence. As her psoriasis gradually began to spread, Carrie began to make efforts to treat it in accord with her belief system, which centred around a holistic, natural therapies-based approach, and with the hope that everyone had been wrong and a cure did in fact exist. At this point, her self-confidence was affected but not too dramatically, and she still held hope that clearance was possible. Yet, as the severity of her psoriasis worsened, it began to feel as if it was taking on a life and power of its own, and Carrie began to feel more and more powerless in its face. Her efforts to try and hide her psoriasis and keep up with physical maintenance became all consuming and she felt she was using all her energy for this purpose, to the point where she felt she was no longer living life. She began to see herself primarily as the psoriasis, not as a person. When she began to experience severe bodily aches and pains, she felt as if her body was breaking down. Ultimately, Carrie reached a point where she felt that life was not worth living unless she was free of psoriasis, and this made her decide she would do anything necessary to have clear skin. This meant compromising her beliefs and values around systemic and biologic drugs, and putting herself through two years of trialing medications and dealing with their side effects. Having had repeatedly negative experiences with doctors up until this point, she decided to seek a dermatologist through the private health system who had been recommended to her. For

Carrie, whether she had a future or not was entirely dependent on the success or failure of the treatments. At the same time, she held onto her conviction that her psoriasis was caused by underlying personal issues that she must deal with if she was ultimately going to cure herself of her psoriasis; in a catch-22, these issues felt impossible to deal with while psoriasis was present. Finding eventual success with one of the biologic treatments has given Carrie her life and, to a degree, her sense of identity back. But she sees the treatment as a kind of band-aid, and she lives conscious of the possibility that psoriasis could return at any time. By giving her near-clear skin, the treatments have allowed her some space to strengthen herself from within, so that if it does return, she will feel stronger in response to it. She tries not to dwell on how bad it has been for her, but does try and reflect on the past in order to have gratitude for the present.

Sally

Sally is in her mid-60s and is happily married with two adult children and a baby grandchild to dote on. She has a full, active life; she has chosen to work in a teaching role past retirement age, and she loves the outdoors, gardening, reading, and spending time with her family. Sally comes across as confident and optimistic.

Sally's psoriasis history

Sally developed psoriasis at the age of 33, which followed a diagnosis of Bell's Palsy after the birth of her second child. Her psoriasis has been limited to her scalp, in an area that she had injured during a motor scooter accident. The main issues for Sally with regards to her psoriasis are the itchiness and heat that occur during flare-ups. Flare-ups tend to happen around two or three times a week and are brought on by being hot, or worry/anxiety.

Sally's storyline

When Sally was diagnosed with psoriasis, she needed to understand why she had developed it. She identified with the doctor's suggestion that it could be linked to her anxiety, but as this did not completely explain it for her, she developed her own theories – perhaps related to post-partum issues, perhaps to a concussion she'd received – and this helped her to make sense of it for herself. Initially, Sally did not believe that there was no cure, and was determined to find a treatment that worked, but as she got older and treatments had been continually unsuccessful, she started to accept it was true there was no cure. This acceptance became important in shaping the attitude Sally took towards her psoriasis; she realised she just had to put up with it and manage it the best way that she could, even though she knew life would be better without it. The key part of management of psoriasis for Sally is simply doing something – having a regime. She regularly visits her dermatologist and applies treatments despite their expense and ineffectiveness in providing relief for her skin. But even using ineffective treatments has some beneficial effect for Sally, as this process helps her feel like she is doing something about her psoriasis. The only directly effective part of Sally's psoriasis management regime is her method of distracting herself to deal with the itch. Her awareness of what triggers her itch, and her ability to reduce her level of suffering helps her to feel some power over her condition, and to bring her psoriasis to a point where she feels she is able to handle it and live with it. Sally has not let her psoriasis interfere much with her life or sense of self. She partially attributes this to the fact it is limited to her scalp, and therefore can't be seen by others, to developing it at 33, when she was already sure of herself rather than in her earlier years, and to not experiencing any negative reactions from others. While the physical nuisance of psoriasis is still a bother to Sally, she has accepted it will always be there, and she has figured out what she needs to do to cope with it in her life.

Penny

Penny is in her late 40s and works as a healthcare assistant. She suddenly lost her relatively young husband a year prior to our interview, and has one adult daughter. Penny has an active social life and some close friends who she can open up to, and she is active within her community. She comes across as a forthright woman who has been through a lot, and who approaches difficulties with the attitude that she has no choice but to get on with things.

Penny's psoriasis history

Penny developed psoriasis around the age of 10 or 11. It began around her ears and scalp, then spread to her arms and legs; today, it can affect any part of her body, including her face. It is widespread and unpredictable, following no apparent pattern or specific triggers. Its most challenging aspects are its intense itchiness, thick scaling and weepiness. Following years of unsuccessfully using topical treatments, she was put on neotigason in her early 20s. This was initially successful then stopped being effective. She was then prescribed methotrexate and has used that intermittently ever since, taking it when her psoriasis flares up and stopping once it is clear. This regime means she might be on it for an average of six months, and then not take it for a couple of years. Her scalp requires the most maintenance, and when her psoriasis is active she has to 'strip' the thick scales from her head on at least a weekly basis. She has recently begun to think her psoriasis is caused by what is put into her body, so while she continues to rely on methotrexate in the meantime, she is hopeful that through having made some major dietary changes, her psoriasis will begin to clear up permanently.

Penny's storyline

Penny has felt judged by others regarding her psoriasis over her entire life, and this has made her feel immensely self-conscious about her skin. As a consequence, she spends a lot of time and energy dressing to hide it, avoiding certain activities and being vigilant about attending to scales that might be visible, such as on her scalp and face. Use of methotrexate has helped her to experience the freedom of having clear skin, but she never feels completely free as she is always aware it will come back at some point, and once it comes back, it can take months to clear it again. She is also conscious of the side effects and risks of methotrexate: she can put up with the nausea, but has to closely manage her proximity to sick people due to its immune-suppressant effects. This means she misses out on experiences she would like to have, such as time with family and events where lots of people are present. After using methotrexate to manage the ups and downs of her psoriasis over more than two decades, the sudden death of her beloved husband becomes a turning point for her in her approach to her overall health. She wants to live a long, healthy life, to eventually find another life partner, and to avoid the potentially damaging effects of being on methotrexate long-term. After reading something that suggests that the answers to overcoming psoriasis may lie in the foods that she eats, she begins to follow a recently popularised way of eating. Although her psoriasis has not improved since then, she still holds out long-term hope this will happen, and since she has experienced dramatic improvements in her general health and weight, she is determined to continue regardless of whether her psoriasis improves or not. As her self-consciousness about her skin persists, even more so now she is single, then she will do whatever it takes to keep her skin as clear as possible, even if it means remaining on some kind of systemic treatment.

Sarah

Sarah is in her late 80s. She lives independently in her own home within a retirement village complex, and is in close contact with her children and their families, who live nearby. She maintains an active life, maintaining connections within the community in which she has always lived, and swimming in her complex's pool. Sarah comes across as a chatty and cheerful woman who doesn't let too much bother her.

Sarah's psoriasis history

Sarah developed psoriasis when she was around 10 years old. The first doctor told her it was a 'germ in her head', while a second opinion confirmed it was psoriasis. It was mainly an issue on her scalp, mostly due to its flakiness and sometimes due to its itch, but it also affected her shins, elbows, back and buttocks. A lot of it was easily hidden under clothing. She has had reasonable success with topical treatments, and has found coal tar gives her the most improvement. She also remembers taking pills for her psoriasis, but she can't remember what they were. They cleared her skin to the point she would think she was cured, but the psoriasis would reappear three months later. The psoriasis on her skin has improved over the years but she still uses coal tar occasionally, if she thinks a patch is particularly bad. In her 30s, she developed a non-painful bump on the side of one wrist, and she was later diagnosed with psoriatic arthritis. She wore blocks under her shoes for a long time because the arthritis was in her feet, but then they improved. Now, her hands are misshapen and have lost some functionality, but the symptoms of arthritis have never caused her pain, and she doesn't take any medication for it.

Sarah's storyline

Sarah's psoriasis was most challenging for her when she was first diagnosed and then through her youth. She saw her initial misdiagnosis of psoriasis as the reason she was prescribed a range of ineffective, messy treatments, the application of which made her life a 'misery'. A second opinion that confirmed it was psoriasis led her to use coal tar, which improved her psoriasis, but its pungent smell was socially challenging to her. The application of treatment was also a burden, and she struggled with having to get up at the 'crack of dawn' to wash her long hair on a daily basis. While having psoriasis did not stop her from doing things while she was young, she did feel self-conscious about it to the extent that she would watch what she wore if she was having a flare-up. However, her self-consciousness and concern with her psoriasis diminished once she was married, and it has not caused her much worry since. Similarly, she has not been too bothered about her psoriatic arthritis, as it did not cause her pain or interfere with her career (despite her being a typist). As an adult, she learned that her uncle had had psoriasis, so to her, this is where hers came from – down the family line. Sarah sees psoriasis as a nuisance, and something that has been a big nuisance in the past, but that has gotten better as she has got older. She believes this is due to her having made inadvertent changes to her diet. She is a bit more diligent in applying treatments if she knows she is going swimming, suggesting psoriasis still has the capacity to bring about mild feelings of self-consciousness. While psoriasis did interfere somewhat on Sarah's daily life when she was young, overall, she does not see psoriasis as having had a major impact on her life.

Victoria

Victoria is a 67-year-old New Zealand woman. She is married to a supportive husband and has three adult children. Victoria is a writer and artist, and spent many years as a teacher. She loves dance, walking and other exercise, and being outdoors amongst the landscape. Victoria has faced several significant hardships during her life, most notably during her difficult childhood and adolescence, and she underwent therapy for many years to work through these. She comes across as eloquent, composed and thoughtful.

Victoria's psoriasis history

Victoria first developed psoriasis on her skin when she was in her mid-twenties, just after the birth of her second child. It was worst on her scalp, with itchiness and flakiness, but also affected her neck and elbows. She tried every cream and ointment available, and Dermol was the only one she didn't have an adverse reaction to, yet it would only relieve the itch temporarily. Around the age of 63, she began to develop physical symptoms, namely stiff joints, difficulty walking and back pain, and after seeing a number of doctors she was eventually diagnosed with psoriatic arthritis. Her symptoms significantly improved once she was put on methotrexate, but worsened again when the dose was lowered too much. Again, it took a number of doctors to realise the dose needed to be increased again, and during this time she suffered debilitating pain. As a result, she is still on strong painkillers at the time of our interview, while she waits for the increased methotrexate dose to make a noticeable difference.

Victoria's storyline

Victoria sees psoriasis as a hereditary condition passed down from her father, and psoriatic arthritis as a consequence of psoriasis. She accepts that there is no cure for either of these conditions, and after having tried many treatments, also accepts that there is nothing that really helps to clear her skin. Having already been through several significant life challenges by the time of her diagnosis, including overcoming the effects of trauma in childhood, the onset of psoriasis feels unfair to her. Yet, she does not let it significantly impact her life, despite causing her to feel self-conscious, embarrassed, and unclean at times, particularly due to the flakes from her scalp. Instead, she maintains the perspective that it could be worse, and is determined to just get on with life, which she does, more and more over time as she develops her sense of independence and engages with her passions. Her feelings of embarrassment and self-consciousness also lessen with time and age. Her diagnosis of psoriatic arthritis much later in life, however, is an unexpected and upsetting blow. She struggles with the idea of yet another setback, after priding herself on all she has overcome. Not only does the arthritis cause progressively worsening physical pain, it threatens to take away the things in life that she loves doing, that she has built her life and, to some extent, her sense of identity around. Although she does not want to use systemic treatments, upon trying them she finds that she can keep up the active lifestyle that makes her feel good and that she takes pride in, and this helps her begin to come to terms with both taking the treatments and having arthritis. But she suffers a major set back when one of her doctors lowers her dose too much, and the pain returns. Going from doctor to doctor, she feels dismissed by one and is misdiagnosed by another, and becomes increasingly frustrated until she finally sees someone who listens to her and realises that her dose needs correcting. The fallout of being without adequate treatment for so long is that the pain greatly interferes with her life, and she feels annoyed at having not received more attentive care, and for having to go on painkillers, which she is not comfortable to do. On the flipside, her frustration means that she reaches a point where she is confident to stand up to her doctors and tell them what she needs, rather than counter-intuitively going along with their decisions. It also reconfirms for her how effective and necessary systemic drugs are for her treatment, and reaffirms her hope that she will be able to live a generally normal life despite having arthritis. Victoria has learned through her experiences that everything has a positive aspect, and both psoriasis, and more notably, psoriatic arthritis, ultimately feature within her life as challenges that she can make the best of and learn to coexist with. She chooses to view her life in its entirety, not focusing on any one

particular aspect, and considers it to be a good life, one which she has earned, and herself as a fortunate woman. As she sees the benefit that can be gained from overcoming life's challenges, she uses her experiences to mentor others, so they can find the motivation to create great lives for themselves, too.

David

David is in his late 30s. He has a supportive wife and two young children, a successful career, and has a love of sports and wine. He went through cancer in his early teens, and overcame it after significant treatment. David comes across as a friendly, easygoing person who has been through a lot, and has learned to appreciate the small things in life.

David's psoriasis history

David first developed tiny spots of dry skin around the age of 24, and he was prescribed a course of oral steroids. He stopped taking these once his skin was clear, and following that he developed widespread psoriasis; in retrospect, he believes this was probably due to oral steroid withdrawal. His psoriasis affected his shins, then his scalp and behind his ears, and then appeared extensively on his torso. The psoriasis on his scalp also began to encroach onto his forehead. He tried a number of topical treatments without success, so ended up trying Traditional Chinese Medicine. This wasn't successful either, but he continued to drink alcohol regularly while taking it, even though he had been told it would hinder the treatment's effectiveness. David experienced a personal breakdown not long after having developed psoriasis, and during his recovery from that, his psoriasis began to improve. Since then, it has remained stable, at a level of severity he is comfortable with, so he doesn't tend to use treatments often. As he has now found a topical treatment that works for him, and he knows he can use this if he feels he needs to get his skin a bit clearer.

David's storyline

David sees psoriasis as a hereditary condition, and he puts the initial onset of it down to oral steroid withdrawal. However, his dominant view of psoriasis is as an external reflection of internal struggles. He experiences a 'gradual explosion' of psoriasis when he moves overseas, and puts this down to being outside of his comfort zone, and to the effects of living an unhealthy lifestyle. While he tries to ignore the fact that his psoriasis, which is hidden under his clothes, is affecting his self-confidence and preventing him from doing things and feeling good about himself, the 'unsightly appearance' of it plays on his mind and gradually chips away at him. Although he wants to improve his psoriasis, and knows that his unhealthy habits are making it worse, he is unwilling to give up his social life to change his way of living, as it is central to his 20-something identity. So, he looks outside himself to other treatments, but their use is futile because he continues with the lifestyle that flares up his psoriasis. As a result, his psoriasis feels like it gets more and more out of control, mirroring the way he has begun feeling about the rest of his life. He is on his way to a personal 'implosion', or breakdown, with his psoriasis both contributing to and being representative of the internal strife that leads to the breakdown. Extracting himself from his negative lifestyle and returning home is David's first step in regaining a sense of control over his life. As he bunkers down and 'unwinds' the thought patterns that led to his breakdown, his psoriasis begins to improve, and this confirms for him the powerful link between his skin and his emotional, mental and physical health. David reaches a point where his psoriasis is stable, and he maintains this over time. He credits this stability to living a happy life, complete with having positive things to focus on such as family, children and a great job. Rather than having to try and ignore his psoriasis as in the past, it has naturally taken a backseat to these other priorities. This is partly as he has a supportive wife and so is not so concerned about his appearance. David's psoriasis now has a positive function: he sees it as an indicator that he needs to look at his lifestyle, such as his diet and exercise, and see what needs improving. He also knows that he has the potential to clear it if he really makes an effort with topical treatments, but clearance is not important enough for him now to bother. He hasn't completely overcome his physical self-consciousness, but knows that it's not the psoriasis that might stop him from doing something, but rather himself. He still finds having psoriasis frustrating, but he now sees it as a frustration he can manage.

Appendices: Study Two



MASSEY UNIVERSITY
COLLEGE OF SCIENCES
TE WĀHANGA PŪTAIAO

Michelle Ingram
IFNHH, Massey University
Private Bag 102 904
North Shore Mail Centre 0745

August 23, 2012

Dr [REDACTED]
Dr [REDACTED]
[REDACTED]
Auckland 0632

RE: Vitamin D and Psoriasis Study

Dear Dr [REDACTED]

I am a PhD Candidate at Massey University working with Dr Paul Jarrett on a study examining the effect of vitamin D₃ supplementation in patients with plaque-type psoriasis. We are attempting to recruit 100 participants for the study and I have attached the details for your information.

We are asking your permission to send you patient information flyers and a small poster that could be displayed in your patient waiting area to help recruitment.

If you are willing to be sent these leaflets please tick the box below and return in the self- addressed envelope.

Thank you for considering this request.

Sincerely,

Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health
Massey University
m.ingram@massey.ac.nz
09 414 0800 extn 41173

Do you suffer from the skin condition Psoriasis?

We are recruiting men and women to take part in a study which will investigate whether vitamin D is an effective treatment for psoriasis.

What is involved?

- This is a randomised trial conducted over 1 year (2012 – 2013).
- You will take a supplement each month (either vitamin D or placebo) and meet with us every 3 months to assess any changes in your psoriasis.
- We will also monitor your vitamin D levels and several other key factors.
- You will find out your vitamin D status at the conclusion of the study.

Like to know more?

Visit our website:

<http://psoriasis.massey.ac.nz>

This study is funded by Lottery Health Research and Massey University, and has been reviewed and approved by the Health & Disability Ethics Committee. NTX/11/07/063

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MASSEY UNIVERSITY

The *Psoriasis* Study



Massey University is seeking people with *psoriasis vulgaris* to take part in a randomised, double-blind, placebo-controlled trial investigating whether vitamin D supplements are an effective treatment for this condition. The research is being conducted in Albany, Auckland over the next 12 months and is part of a PhD in Human Nutrition.

We are looking for 100 male or female volunteers to participate in this study. Criteria for inclusion are:

- Have plaque-type psoriasis (*psoriasis vulgaris*)
- Be 18 years of age or older
- Be a non-smoker
- Not be pregnant, breastfeeding or planning to be in the near future
- Have no kidney or liver problems or diseases
- Not have taken vitamin D supplements in the past 2 months

Study participants will be randomly assigned to take either a 100,000 IU vitamin D₃ supplement or a placebo supplement once a month for one year. There will be twice as many people in the vitamin D group compared to the placebo group. They will be required to attend 5 appointments at Massey University's Human Nutrition Research Unit in Auckland (one every 3 months).

If you have patients with psoriasis who are based in Auckland and may like to be part of this study, please ask them to contact Michelle by email: m.ingram@massey.ac.nz or visit <http://psoriasis.massey.ac.nz> to find out more.

News release



MASSEY UNIVERSITY
TE KUNENGA KI PŪREHUROA

Sonia Yoshioka Braid

09- [REDACTED]

[REDACTED]
news.massey.ac.nz

Tuesday, August 7, 2012

Vitamin D trial hopes to give psoriasis sufferers relief

For the one in 50 adults suffering from psoriasis, finding a treatment that is affordable and socially acceptable is not an easy task, but a team of researchers from Massey University's Vitamin D Research Centre want to see if vitamin D can provide some relief.

Traditional treatment of psoriasis – a chronic, non-contagious inflammatory disease of the skin – can include a topical lotion or creams, pills or injections, or phototherapy, which uses light to treat the condition. These options can be expensive or smelly.

The researchers want to find out if vitamin D supplements are an effective treatment for psoriasis.

“We know that UV radiation increases vitamin D levels, but of course, in winter, when there's less sun about, our vitamin D levels get low,” says research supervisor Dr Pamela von Hurst. “Other options are either expensive, messy or have side-effects. We want to help improve the quality of life for psoriasis sufferers.”

The Auckland-based trial will take place over a one-year period, beginning in August 2012.

PhD research student Michelle Ingram is excited by the potential offered by the study as a low-cost alternative treatment. “Having psoriasis can really affect how people live and interact with others when the condition is active,” she says. “This can be anything from choosing a particular type of clothing to cover it up, to deciding not to go out in public when they feel it's looking really bad. If we can determine the benefits of taking vitamin D supplements, that will give psoriasis sufferers new options in the battle to contain this disease.”

The researchers are looking for 100 Auckland-based psoriasis sufferers aged 18 or older, with plaque-type psoriasis in 'active phase' which has been stable for the past two months. Volunteers must meet certain criteria, and be able to attend five appointments at the Albany-based Human Nutrition Research Unit for assessments and samples. They don't need to have a doctor's referral, and will be screened by a dermatologist before being accepted to the trial.

The Vitamin D Research Centre will form part of Massey's new College of Health in 2013 that will focus on illness and injury prevention rather than cure. The college will bring together specialists from fields ranging from food and nutrition, sport and exercise, rehabilitation, nursing, Maori and Pasifika health, public health, social work, health and safety; as well as those researching the social and economic factors that underpin health and wellbeing.

For further information, or to register your interest, go to: <http://psoriasis.massey.ac.nz>

Page 1 of 1

Friday, November 30, 2012

Summer sun no fun for psoriasis sufferers

For people with active psoriasis, the hot summer months can be an uncomfortable time as they try to hide affected skin under clothing. However, relief may be in sight with an Auckland-based Vitamin D trial currently underway at Massey University's Vitamin D Research Centre, and the research team is looking for more participants.



The trial has received funding from Lottery Health Research, and is being managed by PhD student Michelle Ingram as part of her doctoral thesis. Michelle is excited by the potential an alternative low-cost treatment may offer.

“Traditional treatment of psoriasis can include topical lotions, creams, pills or injections, or phototherapy – which uses light to treat the condition,” she says. “They can be inconvenient, expensive, and increase the risk of other health problems. If we can determine the benefits of taking vitamin D supplements, this could give people with psoriasis another option for treatment.”

Psoriasis is a chronic, non-contagious inflammatory disease of the skin, with an estimated one in 50 adults in New Zealand living with the condition. Plaque-based psoriasis is the most common type, and while it can be managed, there is no known cure.

For the trial, 100 Auckland-based psoriasis sufferers aged 18 or older, with plaque-type psoriasis are needed. Volunteers must meet certain criteria and be able to attend five appointments at the Albany-based Human Nutrition Research Unit for assessments and samples over a one-year period. They don't need to have a doctor's referral and will be screened by a dermatologist before being accepted to the trial.

Ms Ingram says people with psoriasis often avoid normal activities such as swimming and going to the hairdresser when the condition is active, and it can have a significant impact on their self-esteem.

“Simple decisions, like what to wear, can become a major exercise in decision-making. Add that to the daily list of treatments that currently need to be endured, and living with psoriasis becomes very stressful. If we are able to prove that vitamin D can help relieve the symptoms of psoriasis, that's a big step towards helping people with psoriasis lead a more normal life.”

The Vitamin D Research Centre forms part of Massey's new College of Health, which was formally opened recently. It will focus on illness and injury prevention rather than cure. The college will bring together specialists from fields ranging from food and nutrition, sport and exercise, rehabilitation, nursing, Māori and Pasifika health, public health, social work, health and safety, as well as researching the social and economic factors that underpin health and wellbeing.

For further information on the trial, or to register your interest, go to: <http://psoriasis.massey.ac.nz>
Or contact Michele Ingram: m.ingram@massey.ac.nz

Photo caption: Michelle Ingram is seeking participants for her vitamin D psoriasis trial

Wednesday, February 27, 2013

Final intake of participants sought for psoriasis study

Twelve more participants from any ethnicity are needed for a study on the effects of vitamin D on psoriasis, being run at Massey University.

The study, managed by PhD student Michelle Ingram and funded by Lottery Health Research is investigating the benefits of taking vitamin D supplements in the treatment of psoriasis.

“Traditional treatment of psoriasis can include topical lotions, creams, pills or injections, or phototherapy – which uses light to treat the condition,” she says. “They can be inconvenient, expensive, and increase the risk of other health problems. If we can determine the benefits of taking vitamin D supplements, this could give people with psoriasis another option for treatment.”



Psoriasis is a chronic, non-contagious inflammatory disease of the skin, with an estimated one in 50 adults in New Zealand living with the condition. Plaque-based psoriasis is the most common type, and while it can be managed, there is no known cure.

“Anyone can have psoriasis – it isn’t restricted to any ethnicity or age group,” says Ms Ingram. “With the diverse population in Auckland, we would welcome people from all ethnicities to volunteer for this study. We need an additional 12 to sign up now so the study can run to schedule.”

For the trial, 100 Auckland-based psoriasis sufferers aged 18 or older with plaque-type psoriasis are needed. Volunteers must meet certain criteria and be able to attend five appointments at the Albany-based Human Nutrition Research Unit for assessments and samples over a one-year period. They don’t need to have a doctor’s referral and will be screened by a dermatologist before being accepted to the trial.

The Vitamin D Research Centre forms part of Massey’s new College of Health, which was formally opened recently. It will focus on illness and injury prevention rather than cure. The college will bring together specialists from fields ranging from food and nutrition, sport and exercise, rehabilitation, nursing, Māori and Pasifika health, public health, social work, health and safety, as well as researching the social and economic factors that underpin health and wellbeing.

For further information on the trial, or to register your interest, go to: <http://psoriasis.massey.ac.nz>
Or contact Michele Ingram: m.ingram@massey.ac.nz

Photo caption: Michelle Ingram is seeking the last 12 participants for her vitamin D psoriasis trial

Hello,

Thank you for your interest in participating in nutrition-related research at Massey University.

For our next project, we are looking for people who have **psoriasis**, a chronic, inflammatory skin condition. We plan to investigate whether vitamin D supplements can be used as an effective treatment for this disease, which currently has no optimal treatment.

If you or anyone you know has psoriasis, are based in Auckland, and would like to be part of this study, please visit <http://psoriasis.massey.ac.nz> to find out more and get in touch. We require at least 100 people for this study, so we encourage you to pass this on to anyone you think might be interested.

Many thanks!

Michelle Ingram
PhD Candidate
The Vitamin D and Psoriasis Research Team
Institute of Food, Nutrition and Human Health
Massey University
m.ingram@massey.ac.nz



MASSEY UNIVERSITY
COLLEGE OF SCIENCES
TE WAHANGA PŪTAIAO

The Psoriasis Study



INFORMATION SHEET

If you suffer from psoriasis, we would like to invite you to be involved in an intervention trial that will determine whether vitamin D supplements are an effective treatment for your condition. The research is part of a PhD in Human Nutrition, and will take place over a one year period, beginning during winter 2012.

This information sheet provides you with the background to the research and other important details about what is involved, so please read carefully before deciding whether or not to participate.

Introducing the Researchers

The research team for this study includes Michelle Ingram, Dr Pamela von Hurst, Associate Professor Welma Stonehouse, Professor Robert Scragg and Dr Paul Jarrett.

The lead researchers are:

Michelle Ingram

PhD Candidate

Institute of Food Nutrition and Human
Health Massey University

Email: m.ingram@massey.ac.nz

Phone: (09) 414 0800 ext 41173

Dr Pamela von Hurst

Lecturer

Institute of Food Nutrition and Human
Health Massey University

Email: P.R.vonHurst@massey.ac.nz

Phone (09) 414 0800 ext 41205

Why is this research important?

As you are well aware, plaque-type psoriasis (*psoriasis vulgaris*) is a non-infectious, chronic inflammatory condition primarily affecting the skin, but also the nails and joints. Throughout your personal journey with psoriasis, you may have experienced a number of different treatments, including topical creams and lotions, UVB phototherapy, or systemic and biological treatments. Some may have been successful, others not so, and a third group of treatments may have initially shown promise, only to have their effectiveness decrease over time. Even if a treatment has been successful in improving your psoriasis symptoms, perhaps you have felt it was time consuming, expensive, messy to apply, or had unpleasant side effects. It also may have been that you were uncomfortable with undergoing increased UVB exposure in the case of phototherapy, or with using immune-suppressing systemic therapies. While there is a great deal of research directed at uncovering new types of therapies for psoriasis patients, scientists have been thus far unable to create a treatment that is effective, convenient and comes with no risks or side effects.



Vitamin D appears to be a key component in some of the major forms of psoriasis treatment. Some of the creams that are available to you contain a synthetic version of vitamin D that seems to have the same effect in the skin as vitamin D from natural sources. Also, and importantly, the major source of vitamin D is that produced in the skin when it is exposed to UVB light, and it is very likely that the ability of UVB phototherapy to increase vitamin D levels is the reason why it has been used as a treatment for psoriasis for many decades. In fact, research trials that have shown marked improvements in psoriasis following sunlight or UVB exposure have also found a large increase in vitamin D levels. Vitamin D₃ supplements have been used in a wide range of research, and are capable of safely raising vitamin D levels to a similar extent as light therapy. However, no research has investigated whether vitamin D₃ supplements are useful for psoriasis treatment, and we would like to invite you to help us determine this.

Additionally, we are interested in looking at other factors related to psoriasis that might affect vitamin D metabolism, such as body composition and genetics. There are certain genetic variances that have been found to alter a person's response to vitamin D, and we would like to investigate how these variances affect response to vitamin D in relation to psoriasis.

Who are we looking for?

We are looking for 112 healthy male or female volunteers to participate in this study. To take part, you should:

- Have plaque-type psoriasis (*psoriasis vulgaris*) in 'active phase' (preferably medically diagnosed) that has been stable for the past 2 months
- Be 18 years of age or older
- Be a non-smoker
- Not be pregnant, breastfeeding or planning to be in the near future
- Have no kidney or liver problems or diseases
- Not have taken vitamin D supplements in the past 2 months
- Not have undergone UVB phototherapy in the past 2 months

What is going to happen?

After you have read and considered the information provided in this information sheet and have decided to take part in this study, you will be asked to complete a questionnaire to ensure that you fit the inclusion criteria. If you do meet the criteria, you will be invited to attend an appointment at the Human Nutrition Research Unit (HNRU) on the Albany campus at Massey University. This appointment will involve the following:

- You will have a blood sample taken to measure your vitamin D levels and other biomarkers related to the actions of vitamin D, as well as conduct genetic analysis of genes related to vitamin D metabolism.



- The severity and extent of your psoriasis will be assessed using the Psoriasis Area and Severity Index (PASI). You will also have photographs taken of one or two key areas (all photos will be discrete and protect your anonymity).
- You will complete questionnaires about your psoriasis, quality of life and medical history.
- Your weight and body composition will be measured using Bioelectrical Impedance Analysis (BIA). This is a very simple procedure where you stand on a set of foot plates similar to weighing scales, and hold a pair of handles. Your height will also be measured.

Following the first visit, you will be randomly assigned to either the treatment (vitamin D) or placebo group. There will be twice as many people in the vitamin D group than the placebo group. All participants will take a supplement once a month. Neither you nor the researchers will know which kind of supplement you are taking.

You will attend four more appointments (one every three months) throughout the year. Each visit should take approximately one hour.

You will be given the opportunity to ask any questions you may have throughout the study.

Throughout the study period

- You will be sent a reminder to take your supplement once a month.
- You will fill out a short questionnaire on any days you have a cold or flu.

Blood samples

All blood samples will be taken by a trained phlebotomist, processed in the onsite laboratory facilities at the HNRU and frozen at -80°C until they are sent to an accredited laboratory for analysis. Some of the samples may not be analysed immediately after the study and will remain stored at the HNRU in the meantime. Additional analyses of the samples may be undertaken as more information becomes known, but any further analyses will only be conducted as part of this research project.

Genetic testing

Each person has a DNA make-up (their genes) which is different from that of everybody else - except in the case of identical twins. This genetic make-up is a mixture of the genes of our parents. The precise way they are mixed varies from child to child within the same family, so having the same parents does not mean that two children will have exactly the same genes. Inherited genes may explain why some people respond differently to some treatments, or are more prone to disorders, compared to others.

This research will involve the analysis of genes that are involved in vitamin D metabolism. This information is confidential and will not be disclosed, stored, or used in any way without your informed consent.



We have no intention of claiming the right, ownership or property of your individual genetic information or that of your kinship group. You consenting to participate in DNA sampling of the proposed study will not be construed as creating any right or claim on the part of the researcher to your genetic information.

What are the benefits and risks of taking part in this study?

As vitamin D assists calcium absorption, there is a small risk that increasing vitamin D intake could raise calcium in the blood to higher than normal levels. However, the dosage you will take has been safely used in many other trials with no negative effects. We do not expect there will be any adverse influence on calcium levels, but as a precaution we will be closely monitoring your calcium levels during the study.

Some people may experience discomfort when having a blood sample taken, or have a fear of needles. Blood samples will be taken by a trained phlebotomist, who will treat you with respect and take care to accommodate your needs. You may also be accompanied by a support person if required. Occasionally a slight bruising will result, which usually disappears within a day or two. Every effort will be made to ensure your comfort and respect your participation.

The major benefit to you is the potential that we find vitamin D supplements to be a simple, inexpensive and safe treatment for psoriasis. If you are randomised into the placebo group and the treatment is found to be effective, you will be provided with a letter for your GP outlining the study results and recommending you be prescribed vitamin D. You will also have a number of biochemical assessments and two body composition measurements performed during the study at no cost to you. You will have these monitored by trained researchers and health professionals over a year long period, and be provided with results at the culmination of the study. You will also be reimbursed for your travel costs to the HNRU with a \$20 petrol voucher for each of your five visits.

Privacy of data

The data will be used only for the purposes of this project and you will be identified by code number and date of birth only; no individuals will be identified. As the study is a double-blinded trial, neither yourself nor the researchers will know which treatment arm you are in – this will be done by a third party. Only the investigators and administrators of the study will have access to personal information and this will be kept secure and strictly confidential. Results of this project may be published or presented at conferences or seminars, but again, no individuals will be able to be identified in any reports on this study.

The list of participants and their study identification number will be disposed of at the end of the study. Blood samples will be destroyed immediately following analysis unless their return is requested. Any raw data on which the results of the project depend will be retained in secure storage for 10 years, after which it will be destroyed.



Participant's rights

You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- decline to answer any particular question
- withdraw from the study at any time
- ask any questions about the study at any time during participation
- have a friend, family member or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require
- provide information on the understanding that your name will not be used unless you give permission to the researcher
- be given access to a summary of the project findings when it is concluded. Please note there may be a delay between data collection and publication of results.

If you decide to withdraw from the study prior to its conclusion, your data will be excluded from the final analysis.

Project Contacts

If you have any further questions or concerns about the project, either now or in the future, please contact Michelle Ingram on 09 414 0800 ext 41173 or m.ingram@massey.ac.nz.

Committee Approval Statement

This project has been reviewed and approved by the Health and Disability Ethics Committee: Northern X, Reference NTX/11/07/063.

Compensation for Injury

If physical injury results from your participation in this study, you should visit a treatment provider to make a claim to ACC as soon as possible. ACC cover and entitlements are not automatic and your claim will be assessed by ACC in accordance with the Injury Prevention, Rehabilitation and Compensation Act 2001. If your claim is accepted, ACC must inform you of your entitlements, and must help you access those entitlements. Entitlements may include, but not be limited to, treatment costs, travel costs for rehabilitation, loss of earnings, and/or lump sum for permanent impairment. Compensation for mental trauma may also be included, but only if this is incurred as a result of physical injury.

If your ACC claim is not accepted you should immediately contact the researcher. The researcher will initiate processes to ensure you receive compensation equivalent to that to which you would have been entitled had ACC accepted your claim.

Thank you for considering participating in this study!

Vitamin D and Psoriasis Study Screening Questionnaire

Thank you for your interest in our research project.

To ensure that you fit the inclusion criteria of the study, we would appreciate if you could answer the questions below.

If you have any questions or concerns about the form, please feel free to contact Michelle Ingram on email at m.ingram@massey.ac.nz, or leave a voicemail on 09 414 0800 ext 41173.

* 1. What is your name?

First

Last

* 2. What is your gender?

Male

Female

* 3. What is your current age?

* 4. Please provide your contact details:

Daytime phone

Email

Other

Vitamin D and Psoriasis Study Screening Questionnaire

Please answer the following questions related to your psoriasis.

* 5. Do you have plaque-type psoriasis (psoriasis vulgaris)? This type of psoriasis appears as distinct red patches covered in dry, silvery skin (called plaques).

Yes

No

Comment

* 6. Has your psoriasis been diagnosed by a doctor or dermatologist?

Yes

No

Comment

* 7. How serious would you consider your psoriasis to be?

Mild

Moderate

Severe

Comment

* 8. Are you currently undergoing any treatment regime for psoriasis, including use of creams, ointments or lotions?

Yes

No

Vitamin D and Psoriasis Study Screening Questionnaire

9. If you answered yes to the previous question, please provide details below:

Name of treatment 1	<input type="text"/>
Dosage and frequency	<input type="text"/>
Length of time on treatment	<input type="text"/>
Date of last treatment	<input type="text"/>
Name of treatment 2	<input type="text"/>
Dosage and frequency	<input type="text"/>
Length of time on treatment	<input type="text"/>
Date of last treatment	<input type="text"/>
Name of treatment 3	<input type="text"/>
Dosage and frequency	<input type="text"/>
Length of time on treatment	<input type="text"/>
Date of last treatment	<input type="text"/>

Vitamin D and Psoriasis Study Screening Questionnaire

Please answer the following general health-related questions.

* 10. Are you pregnant or breastfeeding, or planning to be in the near future?

Yes

No

Comment

* 11. Do you smoke, or have you recently quit smoking?

Yes

No

Recently quit

If recently quit, please state when:

* 12. Have you ever been diagnosed with any of the following:

	Yes	No
Kidney problems or disorders	<input type="radio"/>	<input type="radio"/>
Liver problems or disorders	<input type="radio"/>	<input type="radio"/>

If yes, please provide more details

* 13. Are you taking any other forms of medication, including traditional or homeopathic medicines?

Yes

No

Vitamin D and Psoriasis Study Screening Questionnaire

14. If you answered yes to the previous question, please specify the name of the medication, the dosage and frequency and the reason you are taking it (i.e. for what health condition):

Medication 1	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Reason for taking it	<input type="text"/>
Medication 2	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Reason for taking it	<input type="text"/>
Medication 3	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Reason for taking it	<input type="text"/>
Medication 4	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Reason for taking it	<input type="text"/>

15. Have you regularly taken any form of supplements, including tablets or drinks, and especially vitamin D or omega-3 supplements, over the past 2 months?

- Yes
 No

16. If you answered yes to the previous question, what are the names, brands and dosages of the supplements you have been taking?

Name of supplement 1	<input type="text"/>
Brand	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Name of supplement 2	<input type="text"/>
Brand	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Name of supplement 3	<input type="text"/>
Brand	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Name of supplement 4	<input type="text"/>
Brand	<input type="text"/>
Dosage / Frequency	<input type="text"/>
Name of supplement 5	<input type="text"/>
Brand	<input type="text"/>
Dosage / Frequency	<input type="text"/>

Vitamin D and Psoriasis Study Screening Questionnaire

17. Do you have any additional comments?

Thank you very much for your time, we will be in touch soon!

Initial response to inquiries about taking part in the study

Dear [name],

Thank you very much for your interest in the Vitamin D and Psoriasis Study.

I have attached an information sheet that describes what will be involved if you are enrolled in the study. Please read this information carefully and do not hesitate to ask if you have any questions.

If you would like to be a participant, please fill out the screening questionnaire found at this web address: <http://www.surveymonkey.com/s/VitDPsoriasis>
This will allow us to determine your eligibility. Please let me know if you cannot access the survey for any reason.

Again, feel free to ask any questions you might have, and I look forward to hearing from you!

Kind regards,
Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health

Response to a person deemed eligible *via* screening questionnaire

Hi [name],

Thanks so much for completing the Vitamin D and Psoriasis Study screening questionnaire. Based on your answers, I would like to invite you to attend an appointment at the Massey University Campus in Albany.

I have some free appointments on Weds 13th and Thurs 14th of February, would you happen to be available on either of those days? If so, please let me know the times that would suit. The appointment will take between 45 minutes and an hour.

Have a great day, and I look forward to meeting you.

Best wishes,
Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health
Massey University Albany

Response to a person deemed ineligible *via* screening questionnaire

Dear [name],

Thank you so much for completing the Vitamin D and Psoriasis Study screening questionnaire. I'm sorry to inform you that you do not meet the eligibility criteria as [reason for exclusion and explanation].

We appreciate your interest in taking part in this study, and wish you all the best.

Kind regards,
Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health
Massey University Albany



Northern X Regional Ethics Committee
Private Bag 92522
Wellesley Street
Auckland 1141
Phone: (09) 580 9105
Fax (09) 580 9001
Email: northernx_ethicscommittee@moh.govt.nz

16 January 2012

Ms Michelle Ingram
Institute of Food, Nutrition and Human Health
Massey University
PB 102 904
North Shore Mail Centre
Auckland 0745

Dear Michelle

Re: Ethics ref: **NTX/11/07/063** (please quote in all correspondence)
Study title: In patients with psoriasis vulgaris, can supplementation with vitamin D3 improve psoriasis as measured by psoriasis area and severity index score? Protocol v#3, 10/11; PIS/Cons v#2, 13/12/11
Investigators: Ms Michelle Ingram (Principal), Dr Pamela von Hurst (Supervisor), Associate Professor Welma Stonehouse, A/Professor Robert Scragg, Dr Paul Jarrett
Locality: Massey University

Thank you for your response received 22 December 2011 with the requested changes and documents. This study has received full ethical approval from the Northern X Regional Ethics Committee. A list of members of the Committee is attached.

Approved Documents

- Protocol number [version 3, dated October 2011]
- Information sheet/Consent form version [2, dated 13/12/11] with the following changes
 - o please insert date of Information sheet in paragraph 1 of consent form.
 - o please include in the information sheet mention of GP being informed as this was mentioned in the consent form (page 1, last line)
- Example of label for vitamin D (received 22/11/11)
- Email advertising [version 2, dated 13/12/2011]
- Poster advertising [version 2, dated 13/12/2011]
- Questionnaires [v1, 2011-2012]
- Form A declaration form
- Form for registered medicines

This approval is valid until 30 August 2014, provided that Annual Progress Reports are submitted (see below).

The following documents were received and reviewed:

- Letter of Maori support from Dr Lily George
- SCOTT approval
- Locality assessment forms signed by procurement manager, R Garscadden

Access to ACC

For the purposes of section 32 of the Accident Compensation Act 2001, the Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out. Participants injured as a result of treatment received in this trial will therefore be eligible to be considered for compensation in respect of those injuries under the ACC scheme.

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
- the method of recruitment
- information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports

The first Annual Progress Report for this study is due to the Committee by **16 January 2013**. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A Final Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.

Requirements for the Reporting of Serious Adverse Events (SAEs)

SAEs occurring in this study must be individually reported to the Committee within 7-15 days only where they:

- are *unexpected* because they are not outlined in the investigator's brochure, and
- are not defined study end-points (e.g. death or hospitalisation), and
- occur in patients located in New Zealand, and
- if the study involves blinding, result in a decision to break the study code.

There is no requirement for the individual reporting to ethics committees of SAEs that do not meet all of these criteria. However, if your study is overseen by a data monitoring committee, copies of its letters of recommendation to the Principal Investigator should be forwarded to the Committee as soon as possible.

Please see www.ethicscommittees.health.govt.nz for more information on the reporting of SAEs, and to download the SAE Report Form.

Statement of compliance

The committee is constituted in accordance with its Terms of Reference. It complies with the *Operational Standard for Ethics Committees* and the principles of international good clinical practice.

The committee is approved by the Health Research Council's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990.

We wish you all the best with your study.

Yours sincerely

A handwritten signature in cursive script, appearing to read 'Cheh'.

Cheh Chua
Administrator
Northern X Regional Ethics Committee\

cc: Dr Pamela von Hurst



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16 November, 2011

**TT50-5517
(1233)**

Pamela von Hurst
Massey University
Private Bag 102904
North Shore
AUCKLAND 0745

Dear Ms von Hurst

**Clinical Trial on Vitamin D3 (Cholecalciferol)
Protocol Number: VitaminDAndPsoriasis**

Further to your letter of 13 October 2011 I am pleased to advise you that this clinical trial has been approved by the Director-General of Health.

You are therefore authorised to distribute Vitamin D3 (Cholecalciferol) for the purposes of this clinical trial to the following approved investigator(s):

Approved Investigators	
Name	Site
Michelle Ingram	Human Nutrition Research Unit Massey University Gate 4, Oteha Rohe Campus Albany Highway Albany AUCKLAND

Please note that it is your responsibility to obtain ethics approval before your trial can commence in New Zealand.

Legal reporting and record keeping requirement

It is a requirement of the Medicines Act 1981 that you

1. report the progress of the trial to the Director-General of Health at six monthly intervals;
2. report the results of the trial to the Director-General of Health on completion of the trial;

3. report serious adverse reactions which occur during the trial to the Director-General in accordance with the requirements of the Guideline on the Regulation of Therapeutic Products in New Zealand, Part 11: Clinical trials – regulatory approval and good clinical practice requirements;
4. keep complete and accurate records of all quantities of the trial medicine supplied during the trial;
5. ensure that every label on every package or container of the trial medicine bears the words "To be used by qualified investigators only" or words of similar meaning.

Additional reporting requirements

If a patient of a medical practitioner who is not an investigator is a trial subject, that medical practitioner should be kept informed of the progress of the trial.

Importation of the trial medicine

If requested, you should present this letter to New Zealand Customs as evidence that the Ministry of Health has no objection to the importation of this clinical trial medicine.

In all further correspondence concerning this medicine, please quote the file reference TT50-8741 (1165).

Yours sincerely



Dr Alexander Bolotovski
for Director-General of Health



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Vitamin D & Psoriasis Study

PARTICIPANT CONSENT FORM

This consent form will be held for a period of five (5) years

I have read and I understand the Information Sheet for volunteers taking part in the study designed to investigate whether vitamin D supplements are an effective treatment for psoriasis. I have had the opportunity to discuss this study and I am satisfied with the answers I have been given. I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study. I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time. I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study. I understand that this investigation will be stopped if it should appear harmful to me. I have had time to consider whether to take part in the study. I know who to contact if I have any side effects from the study, or if I have any questions.

- | | | |
|--|-----|----|
| I consent to blood samples being destroyed at the end of the study | Yes | No |
| I consent to blood samples being sent to the study's nominated laboratories | Yes | No |
| I am aware that the study will involve partial analysis of my genetic makeup | | |
| I consent to such an analysis being performed | Yes | No |
| I understand that if I consent to such analysis, no rights will be created for | | |
| the researcher to my genetic information | Yes | No |
| I am aware that the study may involve storage of my genetic makeup, and | | |
| I give my consent to such storage | Yes | No |
| I wish to receive a copy of the results of the study | Yes | No |
| I agree to my GP or other current provider being informed of my participation | | |
| in this study | Yes | No |

(Please turn over)



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Please complete the following if you wish to have an interpreter during this study:

English	I wish to have an interpreter	Yes	No
Deaf	I wish to have a NZ sign language interpreter	Yes	No
Māori	E hiahia ana ahau ki tetahi kaiwhaka Māori/kaiwhaka pakeha korero	Ae	Kao
Cook Island Māori	Ka inangaro au i tetai tangata uri reo	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu	E	Nakai
Sāmoan	Ou te mana'o ia i ai se fa'amatala upu	Io	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Io	Leai
Tongan	Oku ou fiema'u ha fakatonulea	Io	Ikai

I (*full name*) _____ hereby consent to take part in this study.

Date:

Signature:

Full names of researchers:

Michelle Ingram
Dr Pamela von Hurst
Associate Professor Welma Stonehouse
Professor Kerry Chamberlain
Professor Robert Scragg
Dr Paul Jarrett

Contact phone number for researchers:

Michelle Ingram
09 414 0800 xtn 41173

Project explained by:

Michelle Ingram

Project role:

Principal Investigator

Signature:

Date:



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Vitamin D and Psoriasis Study

PARTICIPANT PERSONAL DETAILS

First name: _____

Family name: _____

Preferred name: _____

Date of birth: _____

Street address: _____

Suburb: _____

Phone (home): _____ Phone (mobile): _____

Email: _____

Medical Practitioner: _____

Address: _____

Phone: _____

Would you be interested in taking part in interview-based research about your experiences with psoriasis?

- Yes *If yes, we may contact you during the study period.*
No

Are you happy to be contacted about future research projects within the Institute of Food, Nutrition and Human Health?

- Yes
No



Subject ID

2	2						
---	---	--	--	--	--	--	--

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Vitamin D & Psoriasis Study

Demographics Questionnaire

Please complete the following questionnaire. Fill in the circle completely and answer in BLOCK capital letter please. A researcher is available to help if needed.

Are you (please tick):

- Male
 Female

Which ethnic group do you belong to? Select whichever applies to you (you may fill in more than one circle).

- New Zealand European
 Maori
 Samoan
 Cook Island Maori
 Tongan
 Niuean
 Chinese
 Indian
 Other (Please specify)

Which country were you born in?

- New Zealand
 Australia
 England
 Scotland
 China (People's Republic of)
 South Africa
 Samoa
 Cook Islands
 Other (Please specify)

If you live in New Zealand but were not born here, when did you first arrive to live in New Zealand? eg. 06/2000 - June 2000

		/					
--	--	---	--	--	--	--	--

What area do you live in?

- Urban e.g. Auckland CBD
- Suburban e.g. Grey Lynn, Remuera, Takapuna
- Rural

What is your marital status?

- Married
- Single
- De facto
- Partner but live separately

What is your highest qualification? (Single response)

Don't count incomplete qualifications or qualifications that take less than 3 months of full time study in total.

- None
- Secondary school qualification
- Trade or technical certificate which took more than 3 months full time study
- Diploma (not Postgraduate)
- Bachelors degree, e.g. BA. BSc. LLB
- Bachelors degree with Honours / Postgraduate Diploma
- Masters degree, e.g. MA, MSc
- PhD
- Professional qualification, e.g. ACA, teaching, nursing
- Other (Please specify)

What is your current occupation (the job you work the most hours in)?

- Administrative & Support Services
- Professional, Scientific & Technical Services
- IT & Telecommunications
- Hospitality, Customer Service & Sales
- Agriculture, Forestry and Fishing
- Construction, Automotive & other Trades
- Government Administration & Defence
- Health Care and Social Assistance
- Education & Training
- Arts & Recreation Services
- Labourers / Unskilled work
- Not currently employed (not retired)
- Retired
- Other (Please specify)

Thank you for completing the questionnaire



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Vitamin D and Psoriasis Study
Medical History: Visit 1

Duration of Psoriasis

When did you first notice you had psoriasis?

Total years with psoriasis:

Diagnosed by dermatologist? **Y/N** Name:

Seasonal Variation

Does your psoriasis get worse at any particular time of year? Y / N

If yes, when is that time? *Summer*

Autumn

Winter

Spring

Medical and Family History

Have you ever been diagnosed with any of the following:

	Tick for yes	Comments
Psoriatic arthritis	Y / N	
High blood pressure	Y / N	
Diabetes	Y / N	
Heart disease	Y / N	
Lupus or ME	Y / N	
Rheumatoid arthritis	Y / N	
Tuberculosis	Y / N	
Other	Y / N	

Does anyone in your family (blood relatives) have any of the following conditions that you are aware of? If possible, please provide the following information:

Condition	Y / N	Relationship(s) and age of diagnosis
Psoriasis	Y / N	
Diabetes	Y / N	
Cardiovascular disease	Y / N	

Recent Lifestyle Changes

Have you done anything over the past 3 months that significantly increased or decreased the amount of time you spent in the sun? E.g. went on holiday. Please describe:.....

Have you been ill over the past 3 months? Please describe (what/when/check meds have been recorded):.....

Fitzpatrick Skin Type

Which skin type describes yours best?

Skin Type	Typical Features	Tanning Ability
I	Pale white skin, blue/hazel eyes, blond/red hair	Always burns, does not tan
II	Fair skin, blue eyes	Burns easily, tans poorly
III	Darker white skin	Tans after initial burn
IV	Light brown skin	Burns minimally, tans easily
V	Brown skin	Rarely burns, tans darkly easily
VI	Dark brown or black skin	Never burns, always tans darkly

Concomitant Medication

Are you on any other medication?	Y / N	Date started?	Frequency of use?
a) Beta blockers	Y / N		
b) Lithium	Y / N		
c) Systemic steroids	Y / N		
d) Interferon	Y / N		
e) Antimalarials	Y / N		
f) NSAIDs (e.g. aspirin, ibuprofen)	Y / N		
g) Tetracyclines	Y / N		
h) Other medication (specify)			

Are you currently on any type of treatment for your psoriasis? Y / N

If yes, please describe below:

Topical emollient/moisturizer Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Topical steroid 1 Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Topical steroid 2 Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Topical steroid 3 Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Coal Tar Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Calcipotriol 1 Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Calcipotriol 2 Y / N Name.....
Date started..... Frequency of use.....
Area of body used on..... Last date used.....
Effectiveness.....

Compound mix 1 Y / N Contents.....
 Date started..... Frequency of use.....
 Area of body used on..... Last date used.....
 Effectiveness.....

Compound mix 2 Y / N Contents.....
 Date started..... Frequency of use.....
 Area of body used on..... Last date used.....
 Effectiveness.....

UVB Phototherapy Y / N
 Date started..... Frequency.....
 Dosage/treatment length..... Last treatment.....
 Effectiveness.....

Methotrexate Y / N
 Date started..... Frequency of use.....
 Dosage..... Last date taken.....
 Effectiveness.....

Ciclosporin Y / N
 Date started..... Frequency of use.....
 Dosage..... Last date taken.....
 Effectiveness.....

Acitretin Y / N
 Date started..... Frequency of use.....
 Dosage..... Last date taken.....
 Effectiveness.....

Adalimumab Y / N
 Date started..... Frequency of use.....
 Dosage..... Last date taken.....
 Effectiveness.....

Etanercept Y / N
 Date started..... Frequency of use.....
 Dosage..... Last date taken.....

Psoriasis Assessment Scores

Assessment Method			Score
Physicians Global Assessment (PGA)	Clear	0	
	Almost clear	1	
	Mild	2	
	Mild/moderate	3	
	Moderate	4	
	Moderate/severe	5	
	Severe	6	
Psoriasis Area and Severity Index (PASI)			
Psoriasis Disability Index (PDI)			
Dermatology Life Quality Index (DLQI)			

Anthropometry

Weight (kg)		Height (m)		BMI		BF%	
-------------	--	------------	--	-----	--	-----	--

PASI Score Calculation

Head and Neck (10%)	Score
# palms (0-10)	
Redness (0-4)	
Thickness (0-4)	
Scale (0-4)	
Arms and Shoulders (20%)	
# palms (0-20)	Score
Redness (0-4)	
Thickness (0-4)	
Scale (0-4)	
Nails?	
Trunk (incl. armpits & groin) (30%)	
# palms (0-30)	Score
Redness (0-4)	
Thickness (0-4)	
Scale (0-4)	
Legs and Buttocks (40%)	
# palms (0-40)	Score
Redness (0-4)	
Thickness (0-4)	
Scale (0-4)	
PASI SCORE:	

ERYTHEMA

- 0 = None
- 1 = Light red (mild)
- 2 = Red, but not deep red (mod)
- 3 = Very red (severe)
- 4 = Extremely red (very severe)

THICKNESS

- 0 = None
- 1 = 0.25mm (mild)
- 2 = 0.5mm (mod)
- 3 = 1mm (severe)
- 4 = 1.25mm (very severe)

SCALING

- 0 = None
- 1 = Mainly fine scale, some of lesion covered
- 2 = Coarser, thin scale, most of lesion covered
- 3 = Coarse, thick scale, most of lesion covered, rough
- 4 = Very thick scale, all of lesion covered, very rough

Grading Thickness (Induration)

INDURATION = 0
No Thickness



INDURATION = 1
0.25 mm
MILD



INDURATION = 2
0.5 mm
MODERATE



INDURATION = 3
1 mm
SEVERE



INDURATION = 4
1.25 mm
VERY SEVERE



Grading Scales

SCALING = 0
No Scale



SCALING = 1
Mainly fine scale, some of lesion covered



SCALING = 2
Coarser, thin scale, most of lesion covered



SCALING = 3
Coarser, thick scale, most of lesion covered, rough



SCALING = 4
Very thick scale, all of lesion covered, very rough



Grading Redness (Erythema)

ERYTHEMA = 0
No Redness



ERYTHEMA = 1
Light Red



ERYTHEMA = 2
Red, but not Deep Red



ERYTHEMA = 3
Very Red



ERYTHEMA = 4
Extremely Red





MASSEY UNIVERSITY
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TE WĀHANGA PŪTAIAO

**Vitamin D and Psoriasis Study:
Visit One Letter**

Dear Valued Participant,

Thank you for offering your time to take part in the Vitamin D and Psoriasis Study. Now that you have had your first appointment, **we would like to let you know what will happen next.**

As active psoriasis vulgaris is the major study requirement, the photographs we took will be sent to the study's consultant dermatologist, Dr. Paul Jarrett, for confirmation of your psoriasis.

We will then be in touch to advise if you can be enrolled in the study.

If you are enrolled:

- Your first 3 months' supplements will be couriered to you with instructions and start date.
- We will contact you once a month to remind you to take your supplement.
- We will book your next appointment for 3 months after the first visit. At this visit we will ask about any illnesses, medication changes or major lifestyle changes you have had between visits, so please make a note of these.

Once again, thank you for making the effort to come to Massey University today. If you have any questions at all during this study, please do not hesitate to get in touch.

Yours sincerely,

Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health
Massey University
m.ingram@massey.ac.nz
09 414 0800 extn 41173

The
Psoriasis
Study



25/01/2013

Dear [name],

We are pleased to welcome you as a participant in the Vitamin D and Psoriasis Study. Enclosed with this letter you will find your first 3 months' worth of supplements (a total of 4 capsules). Please carefully follow the instructions below.

Taking your supplements

Please take **2 capsules** anytime on **Friday 1st February**. The capsules should be taken with a large glass of water, with or without food. You will then take **one capsule** on the same day each month for the next year. Thus, you will take capsule/s on the following dates:

	Taken?		Taken?
1 st February (2 capsules)		1 st August (1)	
1 st March (1)		1 st September (1)	
1 st April (1)		1 st October (1)	
1 st May (1)		1 st November (1)	
1 st June (1)		1 st December (1)	
1 st July (1)		1 st January (1)	

You can use this table to keep track of whether you have taken your capsule for each month. I will also send you a text message reminder to take your capsule on each of the days above. If you would prefer a different form of communication for this, please let me know. You will receive the next 3 months' worth of supplements at your next appointment.

Between now and then, **please keep a detailed note of anything that might change for you with regards to treatments for your psoriasis or other conditions**. This includes keeping track of:

- how often you are using a treatment
- any periods of time when you might stop using that treatment
- what areas you use the treatment on (if it's topical).

Please also make a note of what happens to the affected areas while you are using it (i.e. if they improve or not).

Thank you again for your part in this trial, your involvement is greatly appreciated. As always, please do not hesitate to ask if you have any questions.

Yours sincerely,

Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health
Massey University
m.ingram@massey.ac.nz
09 414 0800 extn 41173



Vitamin D and Psoriasis Trial Capsules

ID: 2200100 **DOB: 29/06/1965**
 Distributed by qualified investigators only.
 Keep out of reach of children
 Avoid light. Store below 25°C **Batch 1/4**



Vitamin D and Psoriasis Trial Capsules

ID: 2200100 **DOB: 29/06/1965**
 Distributed by qualified investigators only.
 Keep out of reach of children
 Avoid light. Store below 25°C **Batch 4/4**



Vitamin D and Psoriasis Trial Capsules

ID: 2200103 **DOB: 01/09/1990**
 Distributed by qualified investigators only.
 Keep out of reach of children
 Avoid light. Store below 25°C **Batch 3/4**



Vitamin D and Psoriasis Trial Capsules

ID: 2200112 **DOB: 06/10/1985**
 Distributed by qualified investigators only.
 Keep out of reach of children
 Avoid light. Store below 25°C **Batch 2/4**



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 Distributed by qualified investigators only.
 Keep out of reach of children
 Avoid light. Store below 25°C **Batch 4/4**



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Vitamin D and Psoriasis Study
Medical History: Visits 2 - 5

Your Psoriasis and Other Treatments

Note: Refer back to participants' answers from previous visits to get full details.

Have you noticed any **changes in your psoriasis**? Y / N

(What kind of changes – improved/worsened since last time, when, where).....
.....
.....
.....
.....

Have you noticed any changes in **how often you use your treatments**? Y / N

(Has frequency increased/decreased compared to before, and to what?)
.....
.....
.....

Have you noticed any changes in **where you use your treatments**? Y / N

(Are there any new affected areas, are there any areas which hadn't previously been treated but now are?).....
.....
.....
.....

Have you noticed any change in **how your psoriasis responds to treatments**? Y / N

(Do affected areas respond more or less well to treatments than previously, or the same?)
.....
.....
.....

Recent Lifestyle Changes

Have you done anything over the past 3 months that significantly increased or decreased the amount of time you spent in the sun? E.g. went on holiday. Please describe:.....

.....

Have you been ill over the past 3 months? Please describe (what/when/check meds have been recorded):.....

.....

Concomitant Medication

Has your non-psoriasis medication changed over the last 3 months? Y / N

Name of medication	Changed?	Date(s) started (dd/mm/yy)	Date stopped
Beta blockers	Y / N		
Lithium	Y / N		
Systemic steroids	Y / N		
Interferon	Y / N		
Antimalarials	Y / N		
NSAIDs	Y / N		
Tetracyclines	Y / N		
Other medication (specify)	Y / N		
Name of other:			

Psoriasis Treatment

Has your psoriasis treatment changed since your last visit? Y / N

Treatments added:

Name.....
Date started.....
Date stopped (if applic.).....
Frequency of use.....
Last date used.....
Areas where used.....
Effectiveness.....

Name.....
Date started.....
Date stopped (if applic.).....
Frequency of use.....
Last date used.....
Areas where used.....
Effectiveness.....

Treatments stopped:

Name.....
Date stopped.....
Reason for stopping.....

Treatments stopped:

Name.....
Date stopped.....
Reason for stopping.....

Treatments stopped:

Name.....
Date stopped.....
Reason for stopping.....

Psoriasis Assessment Scores

<i>Assessment Method</i>			<i>Score</i>
Physicians Global Assessment (PGA)	Clear	0	
	Almost clear	1	
	Mild	2	
	Mild/moderate	3	
	Moderate	4	
	Moderate/severe	5	
	Severe	6	
Psoriasis Area and Severity Index (PASI)			
Psoriasis Disability Index (PDI)			
Dermatology Life Quality Index (DLQI)			



Study ID: _____



Completion Questionnaire

1. At this point in the study, do you think you were in the vitamin D group or the placebo group?
(Please circle)

Vitamin D Placebo No idea

Why did you choose this answer?

1a. Did your opinion about what group you were in change during the study period?

Yes No

If so, when and why?

2. Did you ever have any problems taking the capsules?

Yes No

If yes, please give details:

3. Did you experience any negative effects from taking the capsules?

Yes No

If yes, please give details:

4. Did you experience any positive effects from taking the capsules?

Yes No

If yes, please give details:

5. What seems to trigger your psoriasis (if anything)?

5a. Has this changed during the study period?

Yes No

If yes, please give details:

6. What seems to improve your psoriasis (if anything)?

6a. Has this changed during the study period? If so, please give details:

7. Compared to before you started this study, are you now more likely or less likely to use topical or other pharmaceutical treatments for your psoriasis?

More likely Less likely No change

Why did you choose this answer?

7. Overall, how would you rate your experience as a participant in the Psoriasis Study?

Very positive Positive Neutral Negative Very negative

Why did you choose this answer?

8. Do you have any other comments or feedback you would like to share?

Thank you for completing this questionnaire!



MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

The Psoriasis Study



Thank you for being an integral part of this study!

On behalf of the research team, I would like to sincerely thank you for giving us your time and effort as a participant in The Psoriasis Study over the past 12 months. Your contribution to this research has been invaluable, and I have had great pleasure in getting to know you and work with you over this time.

When will you find out the results?

Each participant needs to complete a full 12 months on the study, and the last people are due to finish in March 2014.

The results from your blood tests must be analysed altogether once everyone has completed the study. This is to preserve the study's 'double-blinded' status (meaning neither you nor I know whether you received the vitamin D or the placebo), and to reduce variability in the laboratory results. Thus, the blood and data analysis required to produce the overall results will take a couple of months from March to complete. It will be my total priority to send these through to you as soon as I can.

Unfortunately this also means that I must wait until then to tell you whether you were on the vitamin D or placebo, but have some suggestions of what you can do until then (see below).

You will ultimately receive a report containing your personal results, what group you were in, the overall study results and what it all means.

What can you do from here?

While we can't predict what the final results of this study will be, there is good evidence to support the benefits of increasing vitamin D levels in the blood to >80nmol/L (and up to 150nmol/L), not only for psoriasis but for a wide range of health conditions. The dose of vitamin D used in this study (100,000 IU/month) was chosen because it enables such levels to be achieved.

If you would like to take a vitamin D supplement, New Zealand GPs are able to prescribe a supplement called Cal-D-Forte, which contains 50,000 IU/month of vitamin D. Alternatively, 100,000 IU/month is the equivalent of about 3300 IU/day, and 1000 IU capsules are inexpensively available at any pharmacy.

If you were on the placebo, 3000-4000 IU/day should elevate your vitamin D levels to >80nmol/L over a few months. If you were on the vitamin D, 3000-4000 IU/day should help you to sustain these levels (which you should have achieved while on the study). If you were to get a lot of sun exposure during the summer months (with a minimum of bare arms and legs exposed), you could probably reduce your dosage over that time.

Once again, thank you so much for being part of this experience for the past 12 months. I wish you all the best and will be in touch with the results in the future.

Yours sincerely,

Michelle Ingram
PhD Candidate
Institute of Food, Nutrition and Human Health
Massey University
m.ingram@massey.ac.nz

The Psoriasis Study



Dear [name],

Thank you for participating in The Psoriasis Study at Massey University, and for your patience while the results were generated.

This report includes your individual results, as well as the main findings of the study, set out as follows:

1. **Treatment group**
2. **Psoriasis severity**
3. **Vitamin D levels**
4. **Weight and body fat percentage**
5. **Main findings of the study**
6. **Suggested vitamin D levels**

1. Treatment group

There were 67 people taking vitamin D and 34 people taking an identical placebo.

You were on the Placebo capsule.

2. Psoriasis Severity

Psoriasis severity was measured by PASI score. 'PASI' is an acronym for Psoriasis Area and Severity Index. A PASI score is calculated based on a visual assessment of psoriasis, and takes into account the degree of redness, scale, thickness and size of plaques across different areas of the body. PASI scores can range from zero (no active plaques) to 72 (complete body coverage). The definition of 'mild', 'moderate' and 'severe' psoriasis differs between researchers; in this study we used the ranges suggested by dermnet.org.nz, which are <7 (mild), 7-12 (moderate) and >12 (severe).

The PASI is the most commonly used tool for assessing psoriasis in research studies, and is probably the best tool that is available at this time. However, it is important to note that it lacks precision, and that scores for the same person can vary greatly if the assessments are done by different people. In this research, we did our best to overcome this obstacle by taking photographs at each visit, which meant that we could have the same researcher determine all PASI scores.

Your PASI scores, as calculated for this study, are in Table 1.

Table 1. PASI scores

	Your score	Average score in your group	Range across all participants
Baseline	3.2	5.2	0.4 - 21.8
3 months	2.7	4.7	0.1 - 22
6 months	2.3	4.6	0.2 - 23.2
9 months	4	4	0.4 - 22
12 months	1.4	3.7	0.1 - 19.4

3. Vitamin D levels

The capsules we used for this study contained vitamin D₃ (cholecalciferol). Vitamin D₃ in a capsule is the same as that produced in the skin when it is exposed to UVB light. Whether it comes from sunlight or supplements, vitamin D₃ is a precursor to active vitamin D. To become activated, it is transported to the liver, where it is converted to serum 25-hydroxyvitamin D₃ (25(OH)D₃), which is the main circulating form of vitamin D, and is also inactive. 25(OH)D₃ is converted to its active form (1,25-dihydroxyvitamin D₃) in the kidney, as well as in various other cells in the body, including skin cells. Active vitamin D is known to regulate cell growth and differentiation (where cells become different types), as well as regulate the immune response, all of which are relevant to psoriasis. Vitamin D acts on skin cells, but only when serum 25(OH)D levels are adequate. The definition of 'adequacy' is still not agreed upon, and there is also no consensus on what optimal levels of vitamin D (serum 25(OH)D) are, however, there is evidence to support the definitions in Table 2:

Table 2. Classification of vitamin D status

<i>Vitamin D Status</i>	<i>Serum 25(OH)D level</i>
Deficient	<50nmol/L
Insufficient	50 – 74nmol/L
Sufficient	≥75nmol/L
Upper Limit	250nmol/L

Your vitamin D levels over the study period are presented in Table 3.

Table 3. Serum 25(OH)D levels

	Your level	Average level in your group	Range across all participants
Baseline	45	62	12 - 137
3 months	78	96	29 - 163
6 months	98	103	48 - 180
9 months	84	103	40 - 180
12 months	84	101	46 - 194

4. Weight and body fat percentage

Higher body fat percentage is associated with higher PASI score (i.e. worse psoriasis) and lower vitamin D levels. The latter is due to vitamin D being sequestered in fat cells, so less is in circulation and available for use by cells.

Your body fat percentage was measured at your first and last visits, and is presented in Table 4, along with your weight for interest.

Table 4. Weight and body fat percentage

	Your weight (kg)	Your body fat %	Average body fat % of participants of same gender
Baseline	92.4	43.6	36.6
12 months	91.6	42.8	35.2

5. Summary of the results

Vitamin D levels

The average (mean) vitamin D level in the vitamin D group had increased from 62nmol/L to 96nmol/L by 3 months, with an average level of 103nmol/L sustained from 6 months onwards.

In the placebo group, we had expected to see no change in vitamin D over the 12-month period. However, average levels increased between 3 months and 6 months (from 59nmol/L to 78nmol/L), which reflected unexplained increases in vitamin D levels in a few participants.

Vitamin D and psoriasis: comparing the two groups

On average, there was an improvement in psoriasis in the vitamin D group over the study period, but there was also an improvement in the placebo group. When we

compared the improvement in psoriasis between the groups, we found no difference. However, because the vitamin D levels of some people in the placebo group had increased, we could not determine whether there was an effect of vitamin D on psoriasis by comparing the improvement between groups. Therefore, we specifically looked at whether higher vitamin D levels (serum 25(OH)D) across the whole group was associated with less severe psoriasis.

Vitamin D levels and psoriasis

We estimated that on average, increasing vitamin D levels were associated with mild improvements in psoriasis. The extent of improvement depended on the severity of psoriasis and was different for each person. These results are based on the relationship between vitamin D and psoriasis *across the whole group of participants*. There appears to be great variability in the effectiveness of vitamin D; in about 1/3 of participants, no association was seen between higher vitamin D levels and improved psoriasis. Therefore, there is no straightforward way of presenting the results (i.e. we cannot say that increasing vitamin D by X will improve psoriasis by Y).

What we are able to do is predict how much psoriasis is likely to improve if vitamin D is increased, based on different initial PASI scores. Because of the variability in responses, we can only apply this at a population (or large group) level rather than for each individual. In general, the more that vitamin D levels increase, the greater the predicted improvement in psoriasis.

Based on our data, we were able to predict how much psoriasis would improve if vitamin D was increased in increments between 25nmol/L and 125nmol/L. The table below presents estimated average improvements based on initial PASI score. Actual improvements for each person vary around these averages.

Table 5. Estimated average improvement in PASI score with different increases in vitamin D level (serum 25(OH)D)

PASI score	Average improvement with increase of 25nmol/L	Average improvement with increase of 125nmol/L
2		
4		
6		
8		
10		
12		
14		

[Values omitted as calculated without accounting for body fat, as in final results].

The higher the vitamin D level and the greater the severity of psoriasis, the more that psoriasis is predicted to improve. However, as you may infer from the results

above, the *percentage* improvement may be much greater in those with mild psoriasis than those with more severe psoriasis.

These results support our hypothesis that increasing vitamin D can improve psoriasis, but they have also confirmed what we were aware of from the outset: that there is much that is not known about psoriasis, and why some people respond to treatments while others do not. Similarly, there can be significant differences in the serum 25(OH)D levels that people achieve, even when taking a vitamin D₃ supplement of the same dose.

Other contributing factors

As we know, psoriasis has no single cause and many contributing factors, so it is important that we were able to account for a wide range of possible influences. Other significant factors included gender (psoriasis tends to be more severe in males), starting a new topical treatment in the previous 3 months (which improved psoriasis) and body fat percentage (psoriasis tends to be more severe with higher body fat). We were also able to account for undefined individual differences in psoriasis severity.

6. Suggested vitamin D levels

Regardless of the effect vitamin D has on your psoriasis, there are a number of reasons to ensure your vitamin D status is adequate. Low vitamin D levels have been associated with increased risk for a number of chronic health conditions, including osteoporosis, cancer, diabetes/insulin resistance, high blood pressure and cardiovascular disease (Heaney, 2008). Vitamin D levels of at least 80nmol/L, and perhaps at least 120nmol/L have been suggested to ameliorate this risk.

The dose of vitamin D we used in this study (100,000 International Units [IU] per month) was chosen because it has been shown to increase the majority of people's vitamin D levels to ≥ 80 nmol/L (Ilahi, Armas, & Heaney, 2008). 100,000 IU per month is the same as 3288 IU per day.

The only concern that has been raised about oral vitamin D relates to increased calcium levels, as vitamin D has a major role in calcium absorption. It is generally accepted that oral doses of up to 10,000 IU of vitamin D₃ per day (Heaney, 2008) and serum 25(OH)D levels of up to 250nmol/L (Hollis, 2005) are safe, with both of these likely to be conservative estimates.

While the predicted improvements in psoriasis in this study are relatively mild, it is promising to see that psoriasis continues to improve as vitamin D levels get higher. A recent pilot study has shown promising results at very high doses of vitamin D₃ (Finamor et al., 2013); hopefully this will lead to another randomised controlled trial at higher doses than we used on this study, in which greater benefits may be seen.

Thank you again for your invaluable part in this research. If you have any questions, you are welcome to send me an email.

Kind regards,

Michelle Ingram
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College of Health
Massey University
Email: m.ingram@massey.ac.nz

On behalf of The Psoriasis Study Research Team.

We are grateful to Lottery Health Research for providing funding for this study.

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**Title: VITAMIN D SUPPLEMENTATION IN PSORIASIS: CHANGE IN
SERUM 25-HYDROXYVITAMIN D AND PREDICTORS OF CHANGE**

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ABSTRACT

Increasing systemic vitamin D may benefit psoriasis. 200,000 International Units (IU) of vitamin D₃ (cholecalciferol), then 100,000 IU/month should elevate and maintain serum 25-hydroxyvitamin D (25(OH)D) ≥ 80 nmol/L in most people. To characterize change in serum 25(OH)D concentration in people with psoriasis following this dosing regime, and to identify predictors of change, men and women (N=65) with mild ($n=50$), moderate ($n=9$) and severe ($n=6$) psoriasis took 200,000 IU of cholecalciferol at baseline (BL), then 100,000 IU/m for the next 11m. Serum 25(OH)D and psoriasis severity were assessed at BL, 3m, 6m, 9m and 12m. Anthropometrics (including percent body fat), high-sensitivity C-reactive protein (hsCRP), family history of psoriasis, age of onset and presence of psoriatic arthritis were also assessed. Serum calcium and albumin were measured to monitor safety. Primary outcomes were a) change in 25(OH)D from BL and b) predictors of change in 25(OH)D between BL and 3m and BL and 12m. Serum 25(OH)D rose from a BL concentration of 62 ± 26 nmol/L (range 12 – 137 nmol/L) to 96 ± 26 nmol/L at 3m ($P < 0.001$), and plateaued around 103 ± 29 nmol/L from 6m to 12m. Mean change in 25(OH)D between BL and 3m was 35 ± 23 nmol/L (range -14 – 87 nmol/L). Only 58.6% sustained ≥ 80 nmol/L for at least 9m. Together, BL 25(OH)D, gender and body fat percentage accounted for around 37% of the variance in change in serum 25(OH)D at 3m, with BL 25(OH)D the most important determinant ($b = -.49$ [95% CI -.69, -.30], $P < 0.001$). Body fat percentage was the most important predictor of change between BL and 12m ($b = -1.74$ [95% CI -2.46, -1.02], $P < 0.001$), with age an additional factor. Psoriasis severity, hsCRP, family history of psoriasis and psoriatic arthritis did not contribute to change in 25(OH)D. These findings reaffirm the variable response of 25(OH)D to cholecalciferol supplementation between individuals, and suggest that key factors affecting response to vitamin D supplementation in people with psoriasis are similar to those in the general population, namely BL concentration, gender, body fat percentage and age.

Keywords: Cholecalciferol, vitamin D₃, psoriasis, response, mega-dose, supplementation

1. INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory condition affecting 2% - 5% of Caucasians [1]. Although it primarily manifests as reddened, raised and scaly lesions on the skin [2], psoriasis is now commonly considered a systemic condition, due to comparatively higher observed levels of pro-inflammatory cytokines [3] and risk of co-morbidities than in the general population [4]. The principal pathophysiological features of a psoriasis lesion are hyperproliferating, abnormally differentiating keratinocytes, angiogenesis, and an immune infiltrate into the epidermis and dermis [2]. Vitamin D is anti-proliferative, regulates cellular differentiation and modulates the immune response [5].

200,000 International Units (IU) of cholecalciferol, then 100,000 IU/month for 12 months should elevate and maintain serum 25(OH)D \geq 80nmol/L in most people [6] (Scragg, unpublished results). Recently, we found an association between increased serum 25(OH)D and improvement in Psoriasis Area and Severity Index (PASI) score in 101 people with psoriasis, 67 of whom were on this dosing regime [7]. Thus, it is possible that cholecalciferol supplementation, which raises serum 25(OH)D, may be of benefit for psoriasis. However, improvements in psoriasis were small and varied significantly between individuals, possibly related to the variability in response of serum 25(OH)D to supplementation.

Changes in serum 25(OH)D following long-term cholecalciferol supplementation have not been characterized in people with psoriasis. While body fat percentage/BMI and baseline 25(OH)D concentration [8, 9] have a well established influence on the magnitude of change in 25(OH)D following supplementation, it is not known whether aspects of psoriasis, such as severity or level of systemic inflammation, also have an effect.

This is a secondary analysis of the aforementioned larger study, which investigated the effects of vitamin D supplementation on psoriasis severity [7]. The objectives of this analysis were (a) to determine the change in serum 25(OH)D concentration at 3,

¹ BL, baseline; BMI, body mass index; hsCRP, high-sensitivity C-Reactive Protein; PASI, Psoriasis Area and Severity Index

6, 9 and 12 months after a baseline dose of 200,000 IU of cholecalciferol, followed by 100,000 IU per month, in people with psoriasis; and (b) to identify factors affecting the magnitude of change in serum 25(OH)D concentration between baseline and 3 months, and baseline and 12 months, in people with psoriasis.

2. MATERIALS AND METHODS

2.1 Participants

This analysis was based on data from the treatment arm of the randomized, placebo-controlled trial ($n=67$) [7]. Participants were men and women aged ≥ 18 years with mild ($n=52$), moderate ($n=9$) or severe ($n=6$) chronic plaque psoriasis. Participants were from in and around Auckland, New Zealand. Exclusion criteria were kidney or liver disease, smoking, taking vitamin D supplements ≥ 1000 IU/day during the last 2 months, pregnant or lactating, and undergoing ultraviolet-B phototherapy.

2.2 Vitamin D intervention

Cholecalciferol was in the form of a monthly mega-dose (2.5mg or 100,000 IU/capsule) taken as gelatine capsules, supplied by Tishcon Corporation (New York, USA). This dose equates to 3288 IU/day.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and the New Zealand Health and Disability Ethics Committee (NTX/11/07/063/AM01) approved all procedures involving human subjects. It was registered with the Australian New Zealand Clinical Trials Registry, registration 12611000648921, <http://www.ANZCTR.org.au>). All participants provided informed, signed consent before undergoing any assessments.

2.3 Procedures

Baseline appointments for the first participants took place in June 2012, and the final appointments were in March 2014.

Participants took 2 x 100,000 IU cholecalciferol capsules at baseline, followed by 100,000 IU/month for the next 11 months. They were reminded to take their capsule by text message, and compliance was confirmed *via* response message.

Each participant attended five 3-monthly appointments over a year to account for seasonal variation in serum 25(OH)D, which was measured at each visit. Also assessed at baseline were weight, height, body fat percentage, Psoriasis Area and Severity Index (PASI) score [10], and serum hsCRP, a marker of systemic inflammation. Body mass index (BMI) was calculated using kg/height in m², and categorized as normal weight 18.5-24.9, overweight 25 – 29.9 or obese ≥ 30 [11]. Body fat percentage was categorized for males or females as follows: very lean (5-8% or 15-18%), lean (9-12% or 19-22%), moderate (13-20% or 23-30%), excess fat (21-30% or 31-40%), risky high (>30% or >40%) [11]. PASI scores are classified as mild <7, moderate 7 – 12 and severe >12 [10]. As vitamin D has a key role in calcium absorption, calcium and albumin were assessed at baseline (as reference), 3 and 12 months to monitor for hypercalcemia.

Details pertaining to participants' psoriasis history were also collected, including the number of years with psoriasis, age of onset, whether they had a known family history of psoriasis, and whether they had been diagnosed with psoriatic arthritis. Skin phototype was graded using the Fitzpatrick score, based on skin tone and tendency to sunburn [12].

2.4 Biochemical analyses

Serum 25(OH)D concentration was assayed using ADVIA Centaur Vitamin D Total Assay, Siemens Healthcare Diagnostics Inc. (NY, USA), which has an assay range of 9.2 nmol/L to 374 nmol/L and a CV of 4.8% - 11.1%. Serum calcium and serum albumin were measured with the Dimension Vista System using the CA method and ALB method, respectively (Siemens Healthcare Diagnostics Inc., NY, USA). Serum concentrations of calcium were adjusted for albumin. Biomarker analysis was carried out by an accredited laboratory (North Shore Hospital Laboratory, Auckland, New Zealand).

2.5 Statistical analyses

Baseline characteristics are presented as *n* (%), mean \pm SD for normally distributed variables and median [25th, 75th percentile] for non-normally distributed variables. ANOVA with Tukeys *post hoc* was used to compare 25(OH)D concentration based on season of commencement, baseline 25(OH)D concentration and percent body fat.

Linear mixed models were used to assess change in 25(OH)D following supplementation. Time was included as a fixed factor, and a random intercept was specified for each participant to account for individual differences in baseline 25(OH)D.

Multiple linear regression was used to assess predictors of change in 25(OH)D between (a) baseline and 3 months, and (b) between baseline and 12 months. For each outcome, the following variables were entered into the model using the stepwise procedure: serum 25(OH)D concentration, season, body fat percentage, hsCRP level and PASI score at baseline; age; gender; Fitzpatrick score; known history of psoriasis (yes/no); diagnosed with psoriatic arthritis (yes/no); onset of psoriasis (<40y or >40y) [13]; number of years with psoriasis.

Statistical analyses were conducted using SPSS Statistics v20.0. All reported *P*-values were based on 2-tailed tests. *P*<0.05 was considered statistically significant.

3. RESULTS

3.1 Participant characteristics

The final analysis included 65 participants, as two with mild psoriasis were excluded from the original dataset. The first was missing a baseline 25(OH)D measurement, and the second had dropped out after his 3 month visit, and compliance was questionable based on the decline in 25(OH)D at 3 months.

Baseline characteristics are presented in **Table 1**. Participants were predominantly New Zealand European, and on average were middle-aged and had elevated body fat levels. Ages ranged from 21 to 78 years. Median [25th, 75th percentile] PASI scores fell within the range considered as mild psoriasis (0.1 – 6.9). Nearly three-quarters of participants had early-onset psoriasis, that is, they developed the condition before age forty [14]. There were more males than females. Males were significantly older ($t(63)=2.876$, $P=0.005$), had more excess/risky levels of body fat and higher (i.e. worse) PASI score ($U(1)=192.0$, $Z=-4.274$, $P<0.001$) than females.

Table 1. Participant characteristics at baseline¹

	Male (n=38)	Female (n=27)	Total (n=65)
Age (years)	54.5 ± 12.6	45.2 ± 13.2*	50.7 ± 13.6
Ethnicity		(n=26)	
New Zealand European	33 (86.8)	17 (65.4)	53 (81.5%)
Maori or Pacific	2 (5.3)	2 (7.6)	4 (6%)
Asian	1 (2.6)	0	1 (1.5%)
Other ²	2 (2.6)	7 (26.9)	8 (12%)
Body fat (%)	28.8 ± 7.0	34.7 ± 8.3 ^a	31.2 ± 8.1
Body fat category:*			
Very lean	0	1 (3.7)	1 (1.5%)
Lean	0	1 (3.7)	1 (1.5%)
Moderate	5 (13.2)	5 (18.5)	10 (15%)
Excess fat	19 (50.0)	12 (44.4)	31 (48%)
Risky high	14 (36.8)	8 (29.6)	22 (34%)
BMI (kg/m ²)	28.3 [26.2, 30.0]	24.8 [22.8, 30.5] ^a	27.1 [23.9, 30.1]
BMI category:			
Normal weight (18.5 – 24.9 (kg/m ²))	5 (13.2)	15 (55.6)	20 (30.8)
Overweight (25.0 – 29.9 kg/m ²)	24 (63.2)	5 (18.5)	29 (44.6)
Obese (≥30.0 kg/m ²)	9 (23.7)	7 (25.9)	16 (24.6)
PASI score [†]	5.8 [4.6, 8.9]	3.3 [1.7, 5.2] ^b	5.2 [3.4, 6.7]
Years with psoriasis	18.5 [9.5, 31.5]	18.0 [10.0, 31.0]	18.0 [10.0, 31.0]
Onset <40 years (yes)	25 (65.8)	23 (85.2)	48 (74%)
Serum 25(OH)D (nmol/L)	64 ± 29	59 ± 22	62 ± 26
hsCRP (mg/L)	1.18 [0.68, 3.65]	0.97 [0.42, 2.0]	1.13 [0.62, 2.36]
Known family history of psoriasis (yes)	14 (36.8)	13 (48.1)	27 (42%)
Has psoriatic arthritis (yes)	5 (13.2)	6 (22.2)	11 (17%)
Fitzpatrick skin type			
I	1 (2.6)	0	1 (1.5)
II	6 (15.8)	4 (14.8)	10 (15.4)
III	13 (34.2)	14 (51.9)	27 (41.5)
IV	15 (39.5)	7 (25.9)	22 (33.8)
V	3 (7.9)	2 (7.4)	5 (7.7)
Season of commencement			
Spring or Winter	18 (47.4)	16 (59.2)	34 (52%)
Summer ³	20 (52.6)	11 (40.7)	31 (48%)

¹Data are number (%), mean ± SD or median [25th, 75th percentile]

²'Other' includes American, Australian, Indian, British, South African (all n=1) and European (n=3)

³No participants commenced the study in autumn

*In males or females: very lean (5-8% or 15-18%), lean (9-12% or 19-22%), moderate (13-20% or 23-30%), excess fat (21-30% or 31-40%), risky high (>30% or >40%) [11]

[†]PASI scores are used to classify mild (<7), moderate (7-12) and severe (>12) psoriasis [10]

^aSignificantly different between genders, *P*<0.01

^bSignificantly different between genders, *P*<0.001

BMI, body mass index; PASI, Psoriasis Area and Severity Index; 25(OH)D, 25-hydroxyvitamin D; hsCRP, high sensitivity C-Reactive Protein

3.2 Baseline serum 25(OH)D concentrations

Overall mean serum 25(OH)D concentration at baseline was 62 ± 26 nmol/L (range 12 to 137 nmol/L). Baseline 25(OH)D varied significantly across participants, $\text{var}(u_{0j})=496.78$, $\chi^2(1) = 202.49$, $P<0.01$. Those who began in summer had a significantly higher mean 25(OH)D (76.7 ± 26.4 nmol/L, $n=31$) than those beginning in winter (46.5 ± 17.6 nmol/L, $n=20$) or spring (53.9 ± 18.1 nmol/L, $n=15$), $F(2, 63)=12.602$, $P<0.001$. Fifteen participants had baseline concentrations of >80 nmol/L, 13 of whom began the study in summer. The distribution of baseline vitamin D status was relatively even across the group, with $n=21$ (32%) <50 nmol/L, $n=25$ (39%) $50 - 74$ nmol/L and $n=19$ (29%) ≥ 75 nmol/L.

After adjustment for season, there was a trend towards lower 25(OH)D in those with moderate compared to risky high levels of body fat (77.7 nmol/L [95% CI 62.0, 93.3 nmol/L] vs. 56.2 nmol/L [95% CI 45.4, 67.0 nmol/L], $F(2, 59)=2.578$, $P=0.08$). There were no differences in baseline levels according to gender, age, ethnicity, age of psoriasis onset, Fitzpatrick score or hsCRP status.

Serum 25(OH)D concentrations following supplementation

Mean 25(OH)D rose to 96 ± 26 nmol/L (range 50 – 163nmol/L) by 3 months ($P<0.001$), then 103 ± 29 nmol/L at 6 months ($P=0.165$), and plateaued until 12 months (**Figure 1**).

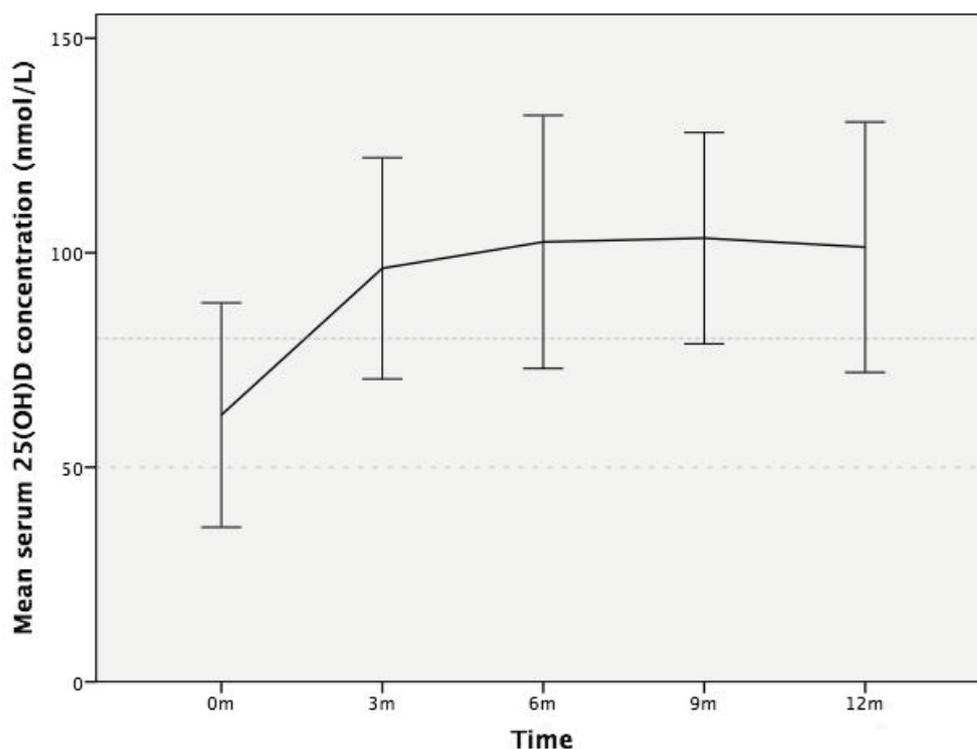


Figure 1. Mean serum 25(OH)D concentrations over 12 months following 200,000 IU of cholecalciferol at baseline, then 100,000 IU/month for 11 months ($n=65$). Error bars are ± 1 SD; reference lines are at 50nmol/L and 80nmol/L.

At each time point after baseline, there were no differences in serum 25(OH)D concentrations based on season of trial commencement (3m: $F(2, 61)=0.897$, $P=0.413$; 6m: $F(2, 59)=1.408$, $P=0.253$; 9m: $F(2, 52)=0.306$, $P=0.738$; 12m: $F(2, 60)=0.130$, $P=0.879$). However, there were differences according to baseline 25(OH)D and body fat. Those for whom 25(OH)D had been <50 nmol/L at baseline had a significantly lower mean concentration than those who had been ≥ 75 nmol/L at each time point (3m, $P<0.001$; 6m, $P=0.016$; 9m, $P=0.002$; 12m, $P=0.001$). At 3m ($P=0.017$) and again at 12m ($P=0.019$), those 50 – 74nmol/L at baseline were also significantly lower than those ≥ 75 nmol/L at baseline (**Figure 2**). Those with moderate levels of body fat had significantly higher levels of 25(OH)D than those with excess fat and risky high levels at 3m ($P=0.01$ and $P<0.001$), 6m ($P=0.011$ and $P<0.001$), 9m ($P=0.016$ and $P<0.001$) and 12m ($P=0.061$ for trend and $P<0.001$) (**Figure 2**).

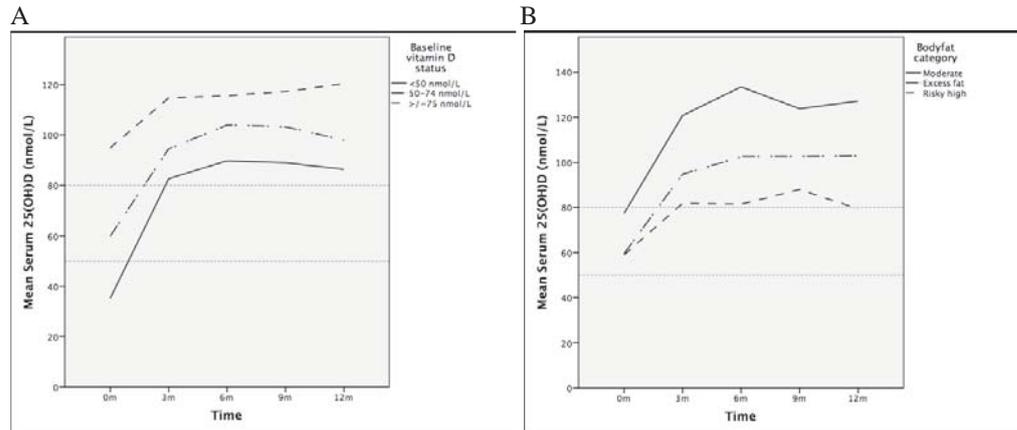


Figure 2. Mean serum 25(OH)D concentrations over 12 months, stratified by (A) baseline vitamin D status, <50nmol/L ($n=21$), 50-74nmol/L ($n=25$), ≥ 75 nmol/L ($n=19$) and (B) body fat category, moderate ($n=10$), excess fat ($n=31$), risky high ($n=22$). Categories with lower body fat omitted as $n=1$ in each. Body fat categories in males or females: moderate (13-20% or 23-30%), excess fat (21-30% or 31-40%), risky high (>30% or >40%). Reference lines are at 50nmol/L and 80nmol/L.

The number of people who achieved serum concentrations of ≥ 80 nmol/L was 45 (69.2%) at 3 months, 47 (72.3%) at 6 months, 46 (70.8%) at 9 months and 47 (72.3%) at 12 months. Thirty-four participants (58.6% of 58 who had 5 measurements) sustained ≥ 80 nmol/L from either baseline or 3 months to 12 months.

Six participants (9.2%; 5 males, 1 female) who completed the study did not reach 80 nmol/L at any time point, as is implied by the error bars in Figure 1 (although two were missing one measurement each, and one was missing two measurements). In three of these participants, there was no discernable change in 25(OH)D concentrations from baseline.

There was very wide variability in both absolute 25(OH)D concentrations and magnitude of change. The widest range of 25(OH)D at any one time point was 46 – 194 nmol/L at 12 months. 194 nmol/L was also the highest concentration achieved, in a participant who had a baseline concentration of 137 nmol/L.

The mean change in 25(OH)D between baseline and 3 months was 35 ± 23 nmol/L (range -14 to 87 nmol/L). The largest increase following supplementation was 87 nmol/L at 3 months, in a participant who had a baseline concentration of 63nmol/L. A decrease from baseline levels was seen in one person at 3 months (-14 nmol/L), four people at 6 months (range -2 to -7 nmol/L), two people at 9 months (-2 and -10

nmol/L) and two people at 12 months (-2 and -21 nmol/L). In all cases, the participant had been in summer at baseline.

3.3 Safety

Serum calcium levels did not exceed the normal range in any person at any time.

3.4 Factors affecting change in serum 25(OH)D concentration

Significant predictors of change in 25(OH)D between baseline and 3 months following vitamin D supplementation were baseline 25(OH)D concentration, gender and body fat percentage. The combination of these factors explained 36.6% of the variance in change ($F(3, 58)=12.716, P<0.001$), with baseline 25(OH)D the most important predictor (**Table 2**). On average, lower baseline 25(OH)D concentration meant a greater magnitude of change from baseline. Lower levels of body fat also predicted larger increases in 25(OH)D by 3 months, while larger increases were predicted for females than males.

The same factors also contributed to the change in 25(OH)D from baseline at 12 months, with age an additional contributing factor. This model explained 37.7% of the variance in change. Body fat percentage was the most important predictor at 12 months, closely followed by gender. Increases in 25(OH)D between baseline and 12 months were greater with increasing age.

The psoriasis characteristics we measured did not influence the magnitude of change in 25(OH)D, nor did skin phototype.

Table 2. Multiple linear regression β -coefficients for predictors of change in 25(OH)D between baseline and 3 months following cholecalciferol supplementation ($n=65$)¹

	β	SE β	Stand. β	Adj. R^2	P-value
Model: Baseline to 3 months²				.366*	<0.001
Intercept	75.62	13.95			<0.001
Baseline 25(OH)D	-.49	.10	-.55		<0.001
Gender (female)	17.46	5.16	.37		0.001
Body fat %	-1.13	.34	-.39		0.001
Model: Baseline to 12 months³				.377**	<0.001
Intercept	56.13	17.85			0.003
Body fat %	-1.74	.36	-.58		<0.001
Gender (female)	24.00	5.91	.48		<0.001
Baseline 25(OH)D	-.42	.10	-.46		<0.001
Age	.58	.21	.31		0.008

¹Stepwise method

²Excluded variables: Age, Fitzpatrick skin type, hsCRP, PASI score, family history of psoriasis, presence of psoriatic arthritis, early/late psoriasis onset, years with psoriasis

³Excluded variables: as for other model except age

* $F(3, 58)=12.716$

** $F(4, 57)=10.233$

4. DISCUSSION

200,000 IU followed by 100,000 IU/m for 12 months safely raised 25(OH)D to ≥ 80 nmol in most of the sample, yet only around 58% of participants maintained this level for at least 9 months. There was very wide variability in both absolute 25(OH)D levels and magnitude of change, with ~37% of the variance in change explained by BL 25(OH)D, body fat %, gender and age. Characteristics of psoriasis had no bearing on change in 25(OH)D, nor did skin phototype.

There is limited research addressing the dose response to monthly mega-doses of cholecalciferol in healthy adults over the longer term. A similar regimen to ours was used by Murdoch et al [15] in 161 healthy adults: 200,000 IU was given at baseline and one month, followed by 100,000 IU per month for a total of 18 months. While baseline 25(OH)D was only marginally higher than in our study (72 ± 22 nmol/L), every participant had reached at least 120 nmol/L by two months and sustained these levels until the end of 18 months. In contrast, only 69% (45 of 65) of participants in our sample had reached 80nmol/L at 3 months. Undoubtedly, the second dose of 200,000 IU was responsible for the higher concentrations in Murdoch et al [14], but the large percentage that did not achieve 80nmol/L by 3 months suggests that participants in our study had a more variable response to supplementation. To illustrate further, only 58.6% of our participants sustained ≥ 80 nmol/L from over 9 or

12 months, and six participants did not achieve 80nmol/L at any time point. All six participants had low baseline 25(OH)D (between 34 and 53nmol/L) and high body fat percentages (31.4% to 43.5%). However, these factors do not completely explain the lack of response, as other participants who did reach 80nmol/L met the same criteria.

More in line with our findings, Castro et al [16] noted large variability in response to 100,000 IU of cholecalciferol, followed by 4000 IU per day for 6 months in a group of asthmatics ($n=201$). Overall, 18% of people did not achieve 75nmol/L during the study period. The mean at 3 months was 105 nmol/L (95% CI 100 – 109 nmol/L), yet the range was extremely large at 16 – 243nmol/L. The largest range in our study was 46nmol/L – 194nmol/L, which occurred at 12 months. Interestingly, there is a link between psoriasis and asthma; both are chronic, immune-mediated inflammatory diseases, and those with psoriasis have an increased risk of developing asthma [17].

Reasons for heterogeneity in response to vitamin D supplementation appear to be multifactorial and thus relatively complex. Differences in response to supplementation have been associated with body fat percentage [9], BMI [18], baseline 25(OH)D concentration and age [8], as well as polymorphisms of genes for the vitamin D binding protein [19] and enzymes involved in vitamin D metabolism [20]. We did not measure genetic factors, and it is likely they contribute to some of the unexplained variance in change. In the case of those in our sample who did not reach 80nmol/L at any time, it is also possible that not all capsules were taken, despite reported compliance.

Baseline 25(OH)D, which is frequently found to affect response to vitamin D supplementation [21] was the most important predictor of change in 25(OH)D in the first 3 months. As the case for other predictors, the reason that baseline 25(OH)D influences change in response to supplementation is not known. It has been proposed that genetic background, or possibly the variability in individual cholecalciferol stores, may contribute to this [21]. On average, lower baseline 25(OH)D concentration meant a greater magnitude of change from baseline. However, it also meant lower absolute 25(OH)D concentrations compared with those who had higher initial 25(OH)D levels. Thus, while those with lower initial levels tend to have a

greater magnitude of change, higher doses of vitamin D are likely to be necessary in this group to achieve the same level of 25(OH)D as those with higher initial levels.

While baseline levels remained an important predictor of change over the long-term (12 months), their relative contribution to change was superseded by body fat percentage as a more important predictor of change by 12 months. That body fat and BMI are significant predictors of response to vitamin D supplementation is well established [8, 9, 22, 23]. The reason for this is not completely understood, but the prevailing hypothesis is that as a fat-soluble vitamin, vitamin D is sequestered by and stored in adipose tissue, of which there is a larger amount in those with higher body fat [24]. We chose to measure and include body fat percentage rather than BMI in our regression model on the basis of this theory.

We found that being of female gender predicted greater increases in serum 25(OH)D in response to cholecalciferol supplementation. Gender differences in response to supplementation have not been well studied, and when gender has been included as a predictor in multiple regression analyses, it has tended not to make a significant contribution (e.g. Fu et al, 2009; [25]). In a cross-sectional study of 2026 morbidly obese patients, Johnson et al [26] found that men had significantly lower mean 25(OH)D concentrations than women (50.0 ± 22.0 nmol/L. versus 536 ± 22.4 nmol/L ($P=0.001$), as well as significantly higher odds of vitamin D deficiency (OR=1.41, 95% CI 1.17 – 1.70, $P<0.001$) after adjustment for intake of vitamin D supplements as well as season, age, current smoking, and BMI. Interestingly, when the authors included waist circumference in the model, the individual contribution of gender to the odds of being vitamin D deficient was slightly reduced, suggesting that the difference in fat deposition patterns between men and women may be a factor in the different response to supplementation. This is consistent with other findings in which obese individuals had lower bioavailability of 25(OH)D due to increased deposition in adipose tissue [24], particularly in visceral fat, which tends to be greater in men [27]. In our findings, although the percentage considered obese according to BMI was similar between men and women, 86.9% of men had a BMI of 25 or higher, compared to only 44.4% of women.

Age was a significant predictor of change in 25(OH)D between baseline and 12 months, with older age predicting larger increases in 25(OH)D. This relationship was also described in a recent meta-analysis of 33 studies of change in 25(OH)D [21]. It has been suggested that this may be due to more frequent low baseline levels in older people [21], yet in our sample, mean 25(OH)D in the youngest tertile was not significantly different to that of the oldest. Like that of Shab-Bidar et al [19], our regression model suggests there is an independent influence of age on change in 25(OH)D, the mechanisms for which are yet to be understood.

Psoriasis has been associated with systemic inflammation, as represented by elevated levels of hsCRP [28]. We included hsCRP in our model as it has the potential to confound vitamin D status [29], however it was not a significant predictor of change in 25(OH)D, possibly because hsCRP levels in our sample were within the normal range.

5. CONCLUSIONS

Supplementation with 200,000 IU then 100,000 IU per month is an effective and safe way to elevate serum 25(OH)D concentrations in people with psoriasis, although there is wide variability in change of 25(OH)D between individuals. Response to vitamin D supplementation in people with psoriasis appears to be influenced by similar factors as for the general population, with greater magnitude of change with increasing age, and with lower levels of body fat percentage and baseline 25(OH)D concentration. However, when baseline 25(OH)D is low, higher doses of vitamin D are probably required to achieve the same 25(OH)D concentrations as when baseline levels are higher. An important focus of future research should be elucidating the underlying mechanisms of the variable responses to vitamin D supplementation.

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